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SACHRP Minutes, October 19-20, 2010

Minutes
Secretary's Advisory Committee on Human Research Protections
March 9-10, 2010 – Washington, D.C.

Voting SACHRP Members Present

Barbara Bierer (Chair), Elizabeth A. Bankert, Carl H. Coleman, David G. Forster, Gary H. Gibbons, Steven Joffe, Lisa Leiden, Patricia A. Marshall, Lainie F. Ross, Stephen O. Sodeke, David H. Strauss

TUESDAY, OCTOBER 19

Welcome: Opening Remarks

Barbara Bierer, M.D., SACHRP Chair

Dr. Bierer welcomed participants to SACHRP's 23rd meeting. She announced that a new ex officio, Jaemie Drake, has been appointed to represent the Department of Homeland Security. Marianna Bledsoe will now be an ex officio representing the National Institutes of Health, replacing Philip M. Budashewitz, who has accepted a position at the Health Research and Services Administration (HRSA).

Dr. Bierer announced that the SACHRP charter has been renewed until October 1, 2012. It has been slightly reworded, but none of the changes relate to the scope of SACHRP's work or its charge.

This will be the last meeting for SACHRP member Liz Bankert. Dr. Bierer observed that Ms. Bankert has been an "incredible gift to committee for long time." She pointed out that Ms. Bankert never missed any part of a SACHRP meeting, showing "unbelievable" leadership and a strong commitment to the work of the committee. Her productive partnership with Dan Nelson as Co-Chair of the Subpart A Subcommittee (SAS) has been a "significant milestone" for SACHRP. While Ms. Bankert appreciates the role of designee to the Institutional Official (IO), Dr. Bierer said Ms. Bankert's heart is with the human subject, a focus exemplified in her principled approach to informed consent.

This may also be the last meeting for David Strauss and Lisa Lieden. However, since it is likely that new members will not be on board by the next SACHRP meeting on March 8-9, 2011, formal goodbyes will be reserved until that time.

Finally, Dr. Bierer announced with regret that this is the last meeting for OHRP staff member Michael A. Carome, M.D., a Captain in the U.S. Public Health Service Commissioned Corps, who has served as the Associate Director for Regulatory Affairs. His contributions over many years were described as "extraordinary." For clarity and subtlety of interpretation, Dr. Carome has been "the" person to turn to." The Chair said that his thoughtfulness, reason, and appreciation of complexity of clinical biobehavioral research will be "sorely missed."

Minutes of SACHRP's last meeting on July 19 and 20, 2010, were approved unanimously.

Report of Issues/Remarks

Jerry Menikoff, M.D., J.D., Director, OHRP

Dr. Menikoff also acknowledged Dr. Bankert's "stupendous" contribution to the work of SACHRP.

He then summarized some highlights of OHRP's work since the last SACHRP meeting. These included:

- Issuing determinations related to allegations regarding dexamethasone use in pregnant women;
- Releasing final guidance on the withdrawal of subjects from research, which has been highly harmonized with FDA guidance;
- Making changes in the procedure for applying for a Federal-wide Assurance (FWA) in order to reduce burdens without lessening protections;
- Released correspondence documenting OHRP's view that several procedures can be considered noninvasive and expeditable;
- Revised Frequently Asked Questions (FAQs) to reflect OHRP's guidance about when an institution is engaged in research and to clarify that compliance actions will be targeted toward entities whose actions were noncompliant.

OHRP has also published information on the 1946-1948 inoculation study in Guatemala conducted by the U.S. Public Health Service. Recent publicity relating to the study gives further impetus to efforts to address issues in international research and problems related to nondisclosure. See: http://www.hhs.gov/1946inoculationstudy/

Dr. Menikoff announced that OHRP is now part of the Office of the Assistance Secretary of Health (OASH), which is a change that is consistent with the way other offices are named. OHRP reports directly to the Assistant Secretary of Health (ASH), and the organizational change now makes this clear.

Summary of Public Comment: Office for Civil Rights Notice of Proposed Rulemaking

Christina Heide, J.D., Senior Health Information Privacy Policy Specialist, OCR

Note: PowerPoints for all presentations are posted on the OHRP Web site. Please see these resources for more detailed information.

Ms. Heide summarized public comments received on aspects of the recent Notice of Proposed Rulemaking (NPRM) pertinent to human subjects protection issued by HHS's Office for Civil Rights (OCR). The NPRM is focused on rules to implement privacy and security provisions of the HITECH Act of 2009, which requires HHS to strengthen protections for privacy and security of protected health information (PHI) under the Health Insurance Portability and Accountability Act (HIPAA) Rules. In addition to the legislatively mandated changes, OCR took the opportunity to address other concerns about the HIPAA Privacy Rule as well.

The current rule requires covered entities to use separate authorization forms for the use or disclosure of PHI for conditioned research activities (e.g., participation in a clinical trial) and unconditioned research activities (e.g., storage of PHI in a biorepository). The research community has expressed concern that requiring multiple forms can be confusing for research participants, is more burdensome in terms of documentation, and is not sufficiently harmonized with the Common Rule. A 2004 recommendation from SACHRP recommended a change in this policy, as did a 2009 report by the Institute of Medicine (IOM).

The NPRM sought public response to a proposal that covered entities be allowed to use a single authorization form for the use and disclosure of PHI for conditioned and unconditioned research activities, provided that the components are clearly differentiated and the individual is provided with an opportunity to opt in to the unconditioned activity. The NPRM also requested comments on ways to differentiate the components. OCR received approximately 60 comments, predominantly in favor of allowing a combined authorization. Most respondents preferred maximum flexibility, though some asked for clear guidance on what is acceptable. A handful of responses were opposed to the change on the grounds that combining forms might be more confusing for research participants.

Another area of concern for researchers has been the lack of harmonization between the Common Rule and HIPAA regarding the authorization requirements for future research. The current interpretation of the HIPAA Privacy Rule is that authorization for research purposes must contain study-specific descriptions of how PHI will be used. Researchers are concerned that this requirement encumbers future research, since some research topics cannot be fully foreseen at the time that authorization is obtained. Furthermore, the Common Rule permits researchers to seek informed consent for future research as long as the research is described in sufficient detail to allow an informed consent. Both SACHRP and IOM also recommended that this area be harmonized.

OCR did not include a specific proposal for a new interpretation of this authorization requirement in the NPRM, but instead asked for comments from the public on how the Privacy Rule might be changed to address concerns about harmonization and workability while ensuring individuals have the information they need to voluntarily and knowingly authorize the future research uses of their health information. Public response was predominantly in favor of allowing maximum flexibility in authorizations for future research. Some asked for clarification of what it means to "adequately describe" the research. Some respondents were in favor of requiring more specificity on future research of "sensitive" PHI. A few opposed the broader authorization on the ground that individuals need study-specific details in order to make informed decisions.

Ms. Heide also noted that OCR asked for input on the appropriate period of protection for the PHI of decedents. Currently, HIPAA generally requires the same protection for the PHI of a deceased individual as a living one, but with special provisions for certain disclosures, such as disclosures for research or to coroners and medical examiners. If authorization is required for a disclosure, HIPAA requires that a covered entity get permission to use a deceased individual's PHI from a person with legal authority to act on behalf of a decedent or a decedent's estate, such as an executor; however, OCR has heard concerns that once the estate is closed, it becomes increasingly difficult to locate someone with legal authority who can authorize the release of data; in effect, the data becomes "locked," and archivists and historians have expressed concern that they cannot access even very old or ancient data that may be valuable for historical

purposes. OCR in the NPRM asked for feedback on the idea of limiting protection to a period of 50 years following the date of death. A majority of commenters supported the proposal, but some suggested using the last date on a medical record instead of the date of death, which might not be known. Others were concerned that the proposed 50 year period was a data retention requirement, which was not the proposal.

Another issue raised for comment in the NPRM concerns the sale of PHI. Consistent with new provisions in the HITECH Act, The NPRM proposed that covered entities be prohibited from disclosing PHI without individual authorization in exchange for remuneration, with a few exceptions. One exception proposed in the NPRM from the HITECH Act is that costs may be charged for preparing and transmitting PHI to a researcher. The NPRM asked for input on the types of costs that should be permitted. Respondents were broadly supportive of a research exception but wanted either a broad interpretation of permissible remuneration or no cost-based restriction at all within the exception.

Under the current rule, covered entities are allowed to disclose PHI to business associates if a contract is in place that protects the PHI. Researchers are not generally considered business associates by virtue of their research activities and the NPRM did not propose to change this. The NPRM proposed to change the definition of business associates to expressly include subcontractors, and Health Information Organizations and Personal Health Record Vendors acting on behalf of covered entities. The NPRM also proposed that business associates, including subcontractors, would be directly liable for security violations and any impermissible uses or disclosures of PHI under the Privacy Rule or their business associate agreement. Given this new direct liability, respondents to the NPRM requested clarification on the definition of business associate in reference to research relationships.

DISCUSSION

Future use of data. With respect to commenters who recommended requiring that authorizations for future research include specific statements or opt outs for sensitive research, Dr. Bierer asked how it would work in the instance in which a person has given permission for data use, then develops HIV or another potentially sensitive condition. Ms. Heide responded that public comments did not suggest how to operationalize such an approach.

Period of protection. Dr. Marshall noted that a period of protection after death is somewhat arbitrary. Also, it is impossible to know what scientific advances might occur in the future that would affect a person's decision. Ms. Heide said she would be interested in hearing about alternative approaches to a limited time period after which HIPAA ceases to apply.

Dr. Goldkind asked for examples of a relevant research project that would want data more than 50 years old. Ms. Heide replied that this proposal is most relevant to historians and archivists . Dr. McNeilly added that some Department of Defense studies look at mental health issues that go back as far as World War I.

Dr. Joffe asked how researchers are allowed to access PHI within the 50-year period, given the difficulty of finding an authorized representative to release it. Ms. Heide explained that the Privacy Rule does not require an authorization or a waiver of authorization from an IRB for research solely on decedents, but rather requires representation by the researcher that he or she is trying to access decedent information for the purpose of research.

Sale of Protected Health Information (PHI). Dr. Strauss asked what language would need to be included in an authorization form to allow the sale of a person's PHI. Ms. Heide said the proposed requirement in the NPRM is that the individual be informed that there is some remuneration involved in the disclosure. Dr. Strauss felt that even if the individual would allow it, the sale of PHI is not necessarily right and is offensive to many people.

Dr. Joffe asked how these provisions would apply to an entity, such as a sponsor, who is buying a bundle of information. Ms. Heide said this was an area of the NPRM on which there was extensive public comment and OCR is reviewing the comments and will address them in the final rule. Dr. Bierer noted that the issue of what happens when PHI is purchased for one reason and is used for another must be addressed.

Business Associates. Dr. Bierer observed that when institutions execute a Business Associate agreement, the agreements do not necessarily spell out what can be done with data on each separate research project.

Report of Subcommittee on Harmonization (SOH): Update

David Forster, J.D., SOH Co-chair; Mark Barnes, J.D., SOH Co-chair; Susan Stayn, J.D., SOH member

Mr. Forster reminded SACHRP that at its initial meeting the subcommittee identified "constellations" of issues where harmonization among the agencies could benefit the regulated community. It then prioritized constellations to work on. Activities completed to date include:

- A recommendation regarding adoption of a single conflict of interest standard across DHHS entities was adopted by SACHRP at its July 21, 2010 meeting.
- The SOH working group on "minor changes in research that are eligible to be expedited" submitted examples and draft Standard Operating Procedures (SOPs) for consideration by OHRP.

Activities in progress include:

- SOH drafted a Request for Information (RFI) to gather public input on harmonization issues. The proposed RFI was submitted to agencies for finalization and release.
- SOH is comparing the Common Rule and FDA regulations. While many differences are based on the agencies' unique roles and are not problematic, SOH plans to consider other issues that do require clarification. SOH will return to SACHRP with recommendations on approaches to harmonize differences.
- SOH is addressing substantial differences among OCR, FDA, and OHRP on the subject of when research begins.
- SOH has given FDA nine examples of research activities that may or may not be "clinical investigations." Its work is intended to clarify when FDA regulations apply. The working group plans to develop an algorithm based on FDA's responses to these examples.
- SOH plans to address harmonization issues related to the definitions of "standard practice" vs. "innovative care," and "research" vs. "clinical investigation." These are especially important in regard to quality assurance and quality improvement activities.

Finally, SOH presented a commentary on the OCR NPRM on HITECH and a proposed approach to harmonizing the definition of a "nonscientist" at this meeting.

Possible future topics include tissue research; the engagement of community in research; consent issues; the application of Subparts B, C, and D; international research; state laws and regulations of non-HHS agencies; incapacitated adults; safety issues; local attitudes; exculpatory language; and a variety of procedural issues, including a possible recommendation to create a single new agency to oversee all human subjects research in the U.S. Dr. Bierer suggested that the last item be considered a priority. What would such an agency look like?

Recommended SACHRP Comments on the HITECH NPRM

SOH prepared a letter to be sent by SACHRP in response to OCR's NPRM on possible rule changes related to HITECH. The letter (Attachment A) addressed topics on which OCR requested comments. Mr. Barnes said that OCR was present during discussions of the letter. Key comments included:

- SACHRP supports the consolidated authorization form, but seeks confirmation that compound authorizations are permitted for combined research activities. It seeks clarification on the effect of revoking one part of the compound authorization. Also, it wants to confirm that waivers of authorization will still be available.
- SACHRP supports the proposal to give entities flexibility in distinguishing between conditioned and unconditioned activities in their forms, but asks HHS to encourage entities to implement the new standard in a way that minimizes duplicative or confusing information for potential research participants..
- SACHRP recommends that HHS clarify that entities have flexibility in applying the existing authorization elements to future and secondary research. Further, it recommends consultation with FDA to ensure that consent or authorization for future or secondary research that meets the standards of the Common Rule and Privacy Rule also meet FDA standards for informed consent. SACHRP recommends "grandfathering" existing studies.
- SACHRP asks OCR to maintain flexibility on the "minimum necessary" standard.
- SACHRP requests that OCR confirm that external IRBs are not "business associates" as this will discourage their use.
- SACHRP seeks clarification on how provisions regarding the sale of PHI apply when health information is disclosed for one purpose to a business associate (such as for quality benchmarking) and the business associate then uses it for unrelated research by itself or other third parties.

INITIAL DISCUSSION OF NPRM LETTER

Information for subjects. Dr. Joffe felt the recommendations should address the need for an information sheet or brochure for subjects. He agreed to draft language for this addition.

Future/secondary research. Mr. Barnes clarified that the intent of the recommendation is to ensure consistency between HIPAA and Common Rule standards. Grandfathering research where an IRB had already approved a consent for the future research was recommended because

the new position is a change. This would mean that a protocol already approved would not have to be reconsidered under the new OCR interpretation of requirements for authorization.

Dr. Marshall felt that some groups might have difficulty understanding a blanket approach to grandfathering in this area that would affect how samples in the past might be used. She suggested including language such as the following: "If relevant, researchers are encouraged to consider some strategy for informing community groups or indigenous groups…." Dr. Bierer observed that SACHRP needs to take a position regarding this area and could either do it in the letter or refer the matter to SAS or SOH.

Dr. Ross was concerned about the implications for group privacy. Policies adopted in regard to PHI should take into consideration the fact that groups may be identified no matter how much data are cleaned, even if individuals are not identifiable. Mr. Barnes felt there was no need to hold up the letter and its recommendations because of the necessity of addressing this issue, which exists regardless of OCR's interpretation of the Privacy Rule.

In regard to disclosure of PHI for research purposes consistent with the authorization (Attachment A, p. 5, second bullet under 2), Dr. Joffe wondered if it was appropriate to leave open-ended the issue of to whom PHI can be provided. One member noted that this was a matter of balance and asked whether it was better for the entity to inform research participants of the breadth of potential recipients at the informed consent stage. SOH preferred this option.

Business Associates. Mr. Barnes emphasized that SOH's concern is how requirements would apply when a covered entity decides to use an external IRB and how this might affect the use of central IRBs. Dr. Bierer raised the issue of which entity would be responsible for a breach in compliance and while this could be addressed in the agreement between the covered entity and the external IRB, the external IRB would not be directly subject to breach notification requirements. She noted that research oversight actions are not covered under HIPAA, and the specific roles and responsibilities of external entities would be defined by inter-institutional agreements.

Acquisition of PHI. Dr. Joffe asked how the proposed changes apply to situations in which PHI is part of a "package" deal with a sponsor and suggested that this be clarified. Ms. Heide said that many respondents had also requested clarification. OCR is considering these comments for purposes of developing the final rule to address when remuneration is involved in a disclosure. Mr. Barnes observed that anti-kickback laws prohibit remuneration for data; rather, remuneration must be based on "reasonable cost." Dr. Bierer suggested writing additional scenarios to be considered by OCR. She also suggested that SACHRP explicitly state that for cases in which PHI is a component of a clinical trial, transmission of PHI should not be considered to be a sale of PHI. Additional scenarios to clarify include:

- The sponsor is not involved in the performance of the clinical trial but will be involved in research on data; the sponsor seeks an agreement that will allow it to import data.
- The sponsor approaches a large health plan and asks for information on adverse events involving its products.

Dr. Bierer expressed appreciation for the enormous amount of work done by SOH and for the critical role played by ex officio SACHRP members. Following the initial discussion of the letter, SOH revised the letter to reflect the input received and presented it for consideration on the second day of the SACHRP meeting.

DISCUSSION OF THE REVISED NPRM LETTER

A revised version of the NPRM letter was presented, and final changes were made by SACHRP prior to approval (see Attachment B). The new letter included three new scenarios under Section V ("No Sale of PHI") and a sentence under Model 3 of the attachment relating to communication with subjects: **"**The consent/authorization form notes that detailed information will be provided in a separate informational brochure."

New scenario beginning with the words, "A pharmaceutical or device company…." SACHRP members noted the need to clarify what happens when research results include PHI. They also asked for confirmation that with authorization, even a very large fee is permissible.

In terms of focusing the scenarios, Ms. Heide explained that today, records held by a covered entity can be disclosed if there is a waiver of authorization; the issue is what happens when payment is changing hands.

Dr. Strauss suggested that SACHRP comment on broader concerns about the secondary use of data originally collected for research. Dr. Bierer suggested that SACHRP may wish to follow up with a panel or separate discussion on this broad topic.

Dr. Bierer observed that the original collection of data might not have occurred in the context of a study.

ACTION

SACHRP unanimously approved a final version of the letter (Attachment B). Two scenarios were included at the end of the letter to clarify recommendations.

Recommendation on the Definition of a Scientist vs. Nonscientist

SOH presented comments and recommendations regarding the definition of scientist and nonscientist for the purpose of determining appropriate members of IRBs as required under 45 CFR 46 and 21 CFR 56. Mr. Forster observed that FDA and OHRP have different definitions of what it means to be a scientist. An earlier review of the same document by SACHRP was found to be too prescriptive; the document was rewritten to be less prescriptive but include the same number of examples.

See Attachment C of this document for the recommendation as presented and Attachment D for the revised recommendation.

DISCUSSION

Mr. Coleman suggested that the recommendation state explicitly that it is possible for someone without scientific training to be considered a scientist. Mr. Forster observed that this statement was included in SOH's original proposal and felt to be too prescriptive. Dr. Strauss commented that there is no "blood test" to determine a committee member's perspective. He observed that some of the most staunchly pro-research members of his institution's IRB are nonscientists.

Dr. Joffe commented that regulatory language refers to the "primary concerns" of the individual as defining whether or not they are a scientist. He said he would like to see a harmonized explanation of "primary concerns." Mr. Coleman said the issue is whether a person feels he or

she is “in the shoes” of the research or the subject. Dr. Ross added that a person’s self-perception might be different in the context of different studies.

Ms. Bankert asked whether a biostatistician should be considered a scientist. She added that people who are trained in behavioral science often fall in a grey area.

SACHRP also considered whether it matters what category of protocol is being considered. Mr. Forster argued that “an anthropologist should be considered a scientist, no matter what type of committee he or she is serving on.” He observed that in most institutions, IRBs review a variety of types of research. Dr. Ross differed, arguing for “wiggle room” in the definition. Dr. Marshall felt the existing wording captured the complexity of the issue. As an anthropologist, she brings the same critical perspective to whatever protocol she reviews.

Dr. Strauss felt that the terms “clearly defined” and “criteria” went too far; the document should focus on principles. He wanted to ensure that IRBs were not held to overly strict guidance. The principles should be clear, but a prescriptive approach could not take into account what is appropriate for each situation.

ACTION

Following discussion, SACHRP made revisions to the text (shown in Attachment D) and approved the revised text with one abstention.

Report of Subpart A Subcommittee (SAS)

Dan Nelson, M.S., CIP, SAS Co-chair; Elizabeth A. Bankert, M.A., SAS Co-chair; David Borasky, M.P.H., CIP, SAS member

Co-Chairs reviewed the subcommittee’s charge, members, and meetings to date.

Preface to FAQs on Biospecimens

SAS presented a proposed preface to be used as a cover note to SACHRP’s series of FAQs when they are forwarded to the Secretary of HHS.

ACTION

With some changes, SACHRP unanimously approved the preface, as shown in Attachment E.

Recommendation Regarding the “Packaging” of FAQ #3 in Biospecimens Series

Co-Chairs presented one “loose end” related to the series of FAQs on biospecimens previously presented to SACHRP and approved. Mr. Nelson noted that when a change was made to the response to FAQ #3, the revisions were labeled as FAQ #3A, even though the scenario being responded to was exactly the same.

> **Scenario (FAQ 3 and 3A):** Blood samples were obtained for research purposes, with informed consent of the subjects, and the original study has been completed. The samples remain under the control of the original investigator. Another investigator wants to use a portion of the remaining samples to perform research completely unrelated to the original study.

If the original consent stated that "…your sample will only be used for research on colon cancer," but the secondary user is interested in studying Alzheimer's disease, can the samples still be used if provided to the secondary user in a coded fashion?

Response (FAQ 3):

The secondary use of de-identified or coded samples is not research involving human subjects under 45 CFR 46. Nevertheless, the original investigator and his/her institution have made an agreement with the subjects about use of their specimens, and have an obligation to honor that agreement.

Institutions should establish mechanisms to determine whether secondary uses are compatible with the original informed consent; this could involve consultation with the IRB that approved the original research, or review by some other body designated for these purposes. Coding should not be used as a means to circumvent the original terms of consent. This is ethically problematic, even if the original project is over and the secondary use is no longer considered to be research involving human subjects.

Additional Response (FAQ 3A): In the case where secondary use of tissue samples is not compatible with the original consent for tissues that are de-identified, coded, or anonymized and are not readily identifiable, the samples are no longer subject to human subject regulations. Thus, there is no regulatory violation.

SAS made the following recommendation:

Recommendation. *In order to minimize confusion by future readers of the SACHRP FAQs on research use of biospecimens, it is proposed that the scenarios currently labeled and presented individually as FAQ #3 and FAQ #3A be recombined into a single FAQ, with a multi-part response.*

DISCUSSION

Mr. Joffee suggested a way of "repackaging" the approved scenarios to clarify the distinction between the two FAQs (adopted and shown as part of the approved recommendation below).

Dr. Strauss expressed concern that guidance was not offered for addressing the scenario. Dr. Menikoff said the situation described should be a regulatory violation, and at some point OHRP may take action to clarify this. He suggested it did not require SACHRP's time at present.

ACTION

With one abstention, SAS approved the recommendation and revised the first paragraph of the response to FAQ 3 as follows to incorporate the new material contained in the recommendation previously labeled FAQ 3A:

The secondary use of de-identified or coded samples is not research involving human subjects under 45 CFR 46. **In the case where secondary use of tissue samples is not compatible with the original consent for tissues that are de-identified, coded, or anonymized and are not readily identifiable, the samples are no longer subject to human subject regulations. Thus, there is no regulatory violation.** Nevertheless, the original investigator and his/her institution have made an agreement with the subjects about use of their specimens, and have an obligation to honor that agreement.

Dr. Sodeke abstained on the grounds that the FAQ appears to indicate that the situation is ethically problematic but not a violation, sending a double message. Dr. Marshall commented that the issue is "huge" and requires public input.

An ex officio member pointed out that it is problematic to place too much emphasis on tracking individual samples; if one is mixed up – as is easy to do – and used in a different way, it seems extreme to make this a regulatory violation.

SAS Work in Progress: Improving the Form and Process of Informed Consent

Mr. Borosky provided a report on SAS's work on informed consent. He explained that SAS's next steps include the following:

- Review FDA guidance (e.g., information sheets; supervisory responsibilities),
- Identify common misperceptions that impact consent form and process, and
- Explore the possibility of a "one-stop shop" for information and materials that were developed to improve the consent form and process.

He added that SAS is considering a recommendation to convene a stakeholders' meeting on informed consent. He noted that meetings held on alternative IRBs proved useful in "getting the word out" regarding what is and is not a compliance issue, and a meeting focused on informed consent might play a similar role. In the discussion that followed, he clarified that the meeting would be used to promote a "shift in thinking" around what was required, helping IRBs to understand how to improve the process of informed consent while staying within the bounds of the Common Rule.

DISCUSSION

Dr. Bierer asked for clarification of the intent and focus of the stakeholder meeting. Mr. Borosky said that SAS hoped the meeting would look at ways of improving consent forms and promoting understanding of consent as a process. He hoped it would help IRBs see that they could improve both and stay in compliance. To succeed, the meeting should attract a fair amount of attention (as the meeting on approaches to IRB review did). Dr. Bierer observed that SACHRP cannot convene a meeting, but it can recommend that someone else do so. The time frame should allow about a year for planning, with a clear focus and view of what it can accomplish.

Mr. Borosky clarified that SAS may be able to develop points to be addressed in guidance as well as model language. Dr. Marshall observed, however, that a variety of models have emerged, as well empirical data pertinent to the identification of best practices. Despite this, Ms. Bankert rejoined, we still don't know enough about what patients really want to know.

CTSA Consortium Report

- ***Daniel Rosenblum,*** *CTSA Clinical Research Management Coordinator, NCRR*
- ***Tesheia H. Johnson, MBA, MHS,*** *Chief Operations Officer, Yale Center for Clinical Investigation, Associate Director of Clinical Research for Yale School of Medicine*
- ***Barbara E. Bierer, MD,*** *Professor of Medicine, Harvard Medical School; Director, Regulatory Knowledge, Harvard Catalyst: Harvard CTSA*

- ***Eric C. Mah, MHS,*** *Director, IRB Administration, Interim Executive Director, Compliance & Integrity Office of Research University of California, Davis*
- ***Nichelle Cobb, PhD,*** *Director, Health Sciences IRBs, University of Wisconsin-Madison*

SACHRP heard presentations from grantees participating in the NIH-funded Clinical and Translational Science Awards (CTSAs). Speakers represented institutions that are using innovative models of IRB review to facilitate collaboration.

Remarks by Daniel Rosenblum: Introduction to Protocol Approval-related Improvements in Clinical Research Management at CTSA Sites

Dr. Rosenblum said there has been considerable progress to date in improving the process for protocol approval at 55 sites throughout the U.S. The presenters will include institutions in which data are available that show positive effects as a result of modifications to the review process. CTSA noted, however, that improvements in quality are hard to define, and the metrics needed to demonstrate value and lower cost are still in development. For the CTSA Steering Committee, the top priority is reducing review time. Meaningful improvement is understood to require:

- Preservation of processes that assure regulatory compliance. Getting sloppy to save time is not an option.
- Management of novel interventions, increasing complexity, and undetermined risks.
- Provision of avenues for local expression of concern for protection of subjects ("it's not just the protocol"). It is very important to some IRBs not to lose control over what is happening in their institutions.
- Development of published metrics that document speedier start-up, improved quality, and reasonable cost.
- Pursuit of the mission of developing an improved academic home for clinical research.

Remarks by Tesheia H. Johnson: Yale Clinical Research Management Challenges: 2008 to Present Day

Ms. Johnson noted that the timeline for research approval, before the changes made through CTSA were instituted, required 80 days from the time someone came to the IRB with a protocol. The changes included improvements by using computer technology to help the IRB process protocols more efficiently. The largest amount of wasted time, however, was the time the proposal spent on the investigator's desk after the IRB returned it with comments. The process changes reduced the amount of time required to complete research approval by 35 days, 18 of which related to reducing the time required by the IRB to complete its review.

Challenges faced included:

- Effecting enterprise-wide change in the silo culture,
- Longstanding structures and the refrain, "w*e have always done it this way,"*
- The natural tendency to look outward toward other entities for change instead of critically examining internal processes,
- A love of wordsmithing, which was viewed as "making a contribution," and

- Getting everyone to the table.

Among a number of other potential applications, Yale is now assessing and adapting the review model to support clinical and translational researchers at the Mayo Clinic, while at the same time importing Mayo Clinic knowledge, expertise and support models to Yale. The Yale program also plans to help the Mayo clinic develop a Community Research Site Toolkit based on the model.

Remarks by Barbara E. Bierer: Development of an IRB Reliance Agreement

Dr. Bierer discussed the ongoing work of the Harvard Catalyst Programs, which includes a number of major institutions (not all of which are affiliated with Harvard). The institution wanted to establish a consensus-based centralized process in a decentralized environment that also respected the fact that each Harvard signatory is a separate legal entity with separate (and mostly accredited) human research protections programs.

Early decisions addressed the definition of "participation" in the CTSA, the nature of authorization, the scope of review, and the definition of "institutional stakeholders," among others. Participants were able to reach common agreement on the following:

1. Scope of agreement. It was agreed that any institution could review and any institution could rely on another institution. There was an embedded expectation that administrators would talk to each other around the protocol and determine which entities were best qualified to review. Whether to rely or review would be determined for each individual protocol.

2. Agreement of "Jurisdiction of PI." The institution that employs the overall PI was understood to have responsibility for protocol review in most instances, unless it was ceded.

3. Process for request of reliance and selection process. Participants agreed, among other things, that an IRB could not reverse its decision to rely on another IRB after seeing its review.

4. Duties and responsibilities to investigators. Institutions developed means of coordinating amendments, adverse or unanticipated events, protocol violations, and other events or developments.

5. Integrating contracting offices. Institutions agreed that IRB approval is not alone the basis for activation of the study. Each institution could request delay of the activation of a study for any reason. including the need for an executed clinical trial agreement.

6. Procedures for managing serious or continuing noncompliance. Institutions agreed on a variety of processes that delineated the responsibility for investigation, including access to records, and determined how findings would be handled.

7. Subject injury and unanticipated problems. Institutions defined the "obligation to report" for both reviewing and relying IRBs, as well as outlining processes for managing injuries.

8.Term and termination. Participants agreed on procedures for terminating their participation.

Dr. Bierer said it took about a year to develop the first set of agreements.

Further information on the Harvard Clinical and Translational Science Center is available at the following site: http://catalyst.harvard.edu

Remarks by Eric C. Mah: Collaborations in Research: The Common IRB Model

Dr. Mah, the IRB Director for the University of California-Davis (UC-Davis), discussed how the Northern California Shriners Hospital for Children and the Veterans Administration (VA) Northern California Health Care System addressed the problem of duplicative IRB review, with the assistance of UC Davis. The VA wished to fund cutting-edge research at the Shriners Hospital.

He noted that assisting the Shriners Hospital with IRB review gave UC Davis a chance to help a neighbor institution and collaborator, but there were concerns: the hospital lacked a clear research compliance program, had no conflict of interest review, and included some researchers who were unaffiliated with UC Davis and unfamiliar with the institution. Therefore, without a clear Memorandum of Understanding (MOU), UC Davis could be exposed to significant liability. Shriners asked UC Davis not only to perform reviews, but also to provide education on human research protection programs. The UC Davis CTSC played a pivotal role in partnering with VA & Shriners, building regional capacity to improve the research enterprise. Its experience was that a number of efficiencies were identified and resources preserved through the collaborative effort and the rights and welfare of research subjects in no way compromised.

Remarks by Nichelle Cobb: The Wisconsin IRB Consortium (WIC): a Model for Multi-Site IRB Review

The WIC needed a year and a half to develop a single authorization agreement for participating institutions, a process made more challenging by the fact that the institutions were arch-rivals engaged in competing for patients. The WIC has now developed SOPs that describe how research teams submit requests to use WIC, established point people at each institution to work with protocols, established quarterly meetings with representatives of the founder institutions, and developed a number of SOPs and shared documents. Where nearly 60 different IRB agreements would have had to exist, there is now only one, which has resulted in a substantial savings in time. A WIC-specific website was developed by one institution and is shared by all four: http://www.wicshare.com/joomla15/

The initiative worked because the leadership at institutions involved were committed to the project, there was inter-institutional trust and flexibility, IRB offices were familiar with one another, legal counsels were able to come to agreement, the key policies were similar across institutions, and that participants had knowledgeable, experienced IRB staff. Also, they did a lot of capacity building to help research teams learn to present multi-site studies to the IRB.

The WIC is now in a transition phase. A challenge to be addressed is the fact that no additional resources were provided to the IRBs for WIC, and the work of reviewing protocols and developing SOPs had to be done in addition to current IRB staff activities. Institutions are now seeking funding for a full-time position to support WIC. They also need resources to help them review the policies of institutions that wish to join to ensure they are in line with the standards set by WIC charter members.

DISCUSSION

A member asked Ms. Johnson whether the agreement among institutions encompasses legal documents. Ms. Johnson said they group is working on contracting now.

A member wondered about the possible disconnect between people on the front lines of research and the people serving on committees. The member also asked how the user community perceives changes. Responses included the following:

- Dr. Bierer said the nature of the complaints has changed, but they still have complaints. There have been practical problems (for example, the IRB reliance agreement does not permit pharmacy to dispense to another institution), as well as issues around cross-credentialing and an employee base that is unionized at some institutions and not others. The program is a good start but is still capturing a minority of protocols and should not be oversold.
- Dr. Mah observed that some faculty members have selective memories. When asked about how current service compares to that of two years ago, they may cite something from 1998.
- Dr. Cobb said she saw little movement as yet.

Dr. Joffe called attention to problems in creating lines of communication between a central IRB and the human research protection programs (HRPPs) at other institutions. Responses included:

- Dr. Cobb observed that each participating institution in WID has a list of things that must be in place to refer protocol review, and this has been helpful.
- Dr. Mah noted that tough areas are AEs and post-approval monitoring and compliance.

Dr. Strauss asked if there were preliminary findings on cost reduction. He also wondered how the models addressed "nuts and bolts," such as uniform case law and policies for review. Responses included:

- Dr. Bierer said that the work done to date has involved only one new full-time staff; the bulk of the work has been accomplished by the participating institutions. Software development has helped to increase efficiency. Cost savings will be related to the prevention of duplicative review.
- Ms. Johnson estimated over a million dollars annually in savings on the part of participating institutions.
- Dr. Cobb reported that institutions meet quarterly to discuss policy positions, and they are learning to respect differences and be flexible.

Overview of the Federation Model for IRB Review of the National Children's Vanguard Study: An Update

- ***Steven Hirschfeld, MD PhD,*** *Captain, U.S. Public Health Service, Associate Director for Clinical Research; Acting Director, National Children's Study*

Dr. Hirschfeld provided an update on the use of the Federation Model of IRB review, as applied and implemented in the National Children's Study (NCS) Vanguard Study. He noted that the Federation of NCS IRBs is modeled after an approach to centralized review for multi-site studies proposed by institutions receiving Clinical and Translational Science Awards (CTSA). It will be implemented as a pilot effort with institutions participating in the NCS and possibly others as well. Tiers of participation are specified in a Memorandum of Understanding (MOU), with each site determining its preferred "tier." An operations center facilitates sharing of information

among all IRBs. A central goal is to reduce duplication of review and the administrative burden at the local level, while maintaining the highest standard of human subject protections review and oversight and building a community of trust.

DISCUSSION

SACHRP members posed questions on the Federation model.

Do you have data on time or quality? Dr. Hirschfield said the metrics are not yet available but are being gathered.

Is this IRB collaboration limited only to the Children's Study? The speaker responded that it can be expanded at any time. A generic toolkit is available to generate MOUs, facilitating the process.

Are there downsides? How do you avoid the "fox guarding the henhouse" scenario? We don't have the field experience to give you the reassurance we would all want. However, if communication channels are trusted and functional, we think this will be a mechanism to improve consistency.

Do you plan to share Adverse Event (AE) reporting? Within NCS, this depends on the tier of the operation receiving reports. Also, there will be some variation depending on arrangements among IRBs.

Public Comment

David Vulcano raised several issues for comment.

He observed that a nonscientific member can over a period of years becomes acclimated to regulatory language and concepts to the point that he or she is no longer functioning as a nonscientist. He wondered if a period of service followed by mandatory retirement would be appropriate. Mr. Forster said the issue was valid, but on the other hand, review becomes easier once IRB members do understand the regulatory framework.

Mr. Vulcano said he had participated in an IRB community in which a university had to withdraw because its insurance company advised it that performing reviews for others was a liability and would result in increased rates; it would mean that the university was now a commercial IRB. He wondered if this was routine. He also wondered how the Stark law and anti-kickback laws in general applied to IRB reviews, noting that lawyers get concerned when institutions do reviews for free, suggesting that there should be reimbursement at fair market value. Currently, he said, both of these situations are obstacles to collaboration among IRBs.

Mr. Mah said his institution receives one FTE as a form of compensation from the Veterans Administration. It does charge for serving as IRB of record for peripherally related studies. Mr. Forster said his institution has insurance and does charge for completing reviews, except in instances of "compassionate use." However, his institution is not a Medicare provider, so Stark does not apply.

Dr. Bierer said that her institution does 300-500 reciprocal agreements annually, but the issue of anti-kickback laws has never been raised. She suspects the risk is small because the institution reviews for a variety of others. She suggested asking the Centers for Medicare and Medicaid Services for clarification on their policy. Dr. Menikoff agreed to follow up.

WEDNESDAY, OCTOBER 20

Remarks/Discussion of Possible Panels

Barbara Bierer, M.D., SACHRP Chair

Dr. Bierer thanked Federal staff for making the meeting possible. She then invited SACHRP members to suggest topics for future SACHRP panels. Members proposed the followed:

- Secondary use of research materials (data and tissues);
- Development of a framework for guidance for IRBs and investigators related to Internet research;
- Development of a framework for guidance on research involving communities, including community-based research;
- Assessment of community risk in behavioral and biomedical research;
- The concept of balance and clinical equipoise;
- Ethical issues in recruitment;
- How to choose a central IRB;
- The meaning of "local context";
- How a focus on compliance drives the behavior of IRBs; and
- How to lessen the regulatory burden for minimal risk research.

Members expressed a strong desire to have time to develop "next steps" in response to panels.

Recently Issued OHRP Documents: Guidance on Subject Withdrawal and Draft Revised FWA

Michael A. Carome, M.D., OHRP, CAPT, U.S. Public Health Service; Associate Director for Regulatory Affairs, Office for Human Research Protections

Dr. Carome provided an overview of two documents recently issued by OHRP:

- Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues, and
- Draft revised Federalwide Assurance (FWA) documents.

Guidance on Withdrawal of Subjects from Research: Data Retention and Other Related Issues

The guidance clarifies that when a subject chooses to withdraw from (i.e., discontinue his or her participation in) an ongoing research study, or when an investigator terminates a subject's participation in such a research study without regard to the subject's consent, the investigator may retain and analyze already collected data relating to that subject, even if that data includes identifiable private information about the subject.

The final guidance includes a recommendation that investigators plan for the possibility that subjects will withdraw from research and that they include a discussion of what withdrawal will mean and how it will be handled in their research protocols and in informed consent documents. Furthermore, the final guidance addresses the question of what investigators, when seeking the informed consent of subjects, should tell the subjects about data retention in the event the subjects withdraw.

Draft Revised Federalwide Assurance (FWA)

Dr. Carome reviewed the following proposed changes to the FWA:

- The current separate FWA forms for U.S. and non-U.S. institutions have been combined into a single form.
- The Terms of Assurance document has been shortened and simplified.
- The current requirement that all IRBs (both internal and external IRBs) relied upon by the institution be specifically designated would be replaced with the requirement that only internal IRBs be specifically designated or that, if an institution does not have an internal IRB, only one external IRB be specifically designated. This change is being made in response to a recommendation from SACHRP.
- The revised FWA form would no longer request submission of the HHS Institution Profile code or the Federal Entity Identification number.
- The revised FWA form would allow the FWA to be signed by the institution's signatory official electronically and eliminate the need to submit a hard-copy signature page by mail or facsimile.
- The standard period of approval for an FWA would be increased from the current 3-year period to a 5-year period.

Dr. Carome then presented the revised form and highlighted changes in the language. The period for public comment period on these revisions closed on October 25. The proposed changes may be reviewed at the OHRP website: http://www.hhs.gov/ohrp/requests/com0910rev.html

DISCUSSION

Guidance on the withdrawal of subjects. Dr. Bierer expressed appreciation for the guidance, which clarified a number of issues. Dr. Strauss said he was comfortable with OHRP's conclusions but asked for the rationale behind the guidance that investigators may retain data in the instances described. He also suggested that the guidance had implications for the informed consent process, in that subjects ought to be informed that their data may be retained even if they decide to withdraw from the research.

Dr. Carome explained that the regulations offer flexibility around what it means to participate in research and do not define the term. Given FDA's position in December 2008 and the desire to harmonize the agency's positions, OHRP concluded that a similar position was appropriate. He also noted that most of the comments OHRP received on the proposed position were favorable. Dr. Menikoff supported this explanation, adding that if investigators do wish to return participant data in research that is not FDA regulated, OHRP's guidance does not discourage them from doing so.

Draft FWA. Mr. Forster commented that many foreign agencies believe that if they do not check the box that indicates they will follow the Common Rule on the FWA form, they do not have to follow the regulations. This is a common misperception. Dr. Carome agreed and said that OHRP has put out a notice to this effect. It has also included a link explaining this in the revised form.

Dr. Joffe said he wondered why there was a place to check for a statement of principles. Dr. Carome explained that the elements an assurance must include are specified in the regulations, but OHRP has tried to make this easier by presenting the requirement as a check-off box.

Dr. Bierer commented that a number of IRB administrators have said that the only way they know that another institution thinks they are relying on them is by getting the an email from OHRP that says they have been listed by that institution. They can then call the institution and ask why it listed them. Dr. Carome said the Common Rule agencies had discussed this issue, but had concluded that it was not a serious problem since OHRP would ask to see a written agreement before holding the institution responsible for any review.

The Chair asked Dr. Carome to explain the value of listing internal IRBs. Dr. Carome responded that it is helpful for the purpose of correspondence. Dr. Menikoff added that it also adds an element of transparency that may be useful to the public. He observed that NIH IRBs are theoretically the IRB of record for thousands of entities; OHRP is well aware that lists of such IRBs are "garbage." In light of this, the proposed changes were suggested by SACHRP, among others.

Dr. Bierer asked whether there was a downside to listing more than one external IRB used by an institution. Dr. Carome said the institution can designate additional IRBs as it wishes, and how many it lists is up to the institution.

Dr. Bierer commented that the only advantage of the previous system was that every time the FWA changed, it was automatically renewed. Having a renewal period of 5 years and a real review is a better system; it should result in a better picture of how IRBs are being used. She said OHRP had done a "masterful" job of writing these documents.

The Use of Deception in Human Subjects Research

- ***Frank Miller, Ph.D.,*** *Faculty, NIH Clinical Center Department of Bioethics*
- ***Joan E. Sieber, Ph.D.,*** *Founder and Editor-in-Chief of Journal of Empirical Research on Human Research Ethics*

Remarks by Franklin G. Miller: Deception and Research: Ethics and Regulation

Dr. Miller defined deception as "deliberately misleading communication about the purpose of research and/or procedures employed." He noted that deception is frequently used in psychology, neuroscience, and behavioral research, but is less common in clinical research. The purpose of deception is to promote scientific validity by enabling investigators to obtain unbiased data about attitudes and behavior in circumstances where truthful disclosure is considered likely to produce biased responses by subjects. He proposed that deception should not be used when nondeceptive alternatives are available and should not be used unless the research has sufficient potential social value to justify the risks associated with deception.

Dr. Miller noted that debriefing sessions can be used to mitigate the harm and wrong of deception by explaining the rationale for the deception. He held that the debriefing should include an offer to withdraw the subject's data from the study if desired. In addition, he proposed the use of "authorized deception" (AD), a procedure in which, prior to the study, subjects are informed that a study will not be described accurately or that some procedures will be deceptive. This provides them an opportunity to decide whether or not to participate on these terms.

Remarks by Joan E. Sieber

Dr. Sieber pointed to four instances in which the use of deception might be appropriate in research:

- For validity: to achieve random assignment and stimulus control.
- To study low-frequency responses.
- To obtain valid data without serious risk to participants.
- To obtain information that people cannot validly self-report.

She felt that deception research is unethical whenever it is used as a way of tricking people into doing something they would not want to participate in. The "surrogate subject method," in which an experiment is described to peers of the proposed subjects to determine how they would feel about participating, is a good way to determine what their attitudes to deception might be in a particular study. She held that study procedures that upset participants may be unethical in some cases.

Dr. Sieber agreed with Dr. Miller that it is possible to devise a consent process that allows subjects appropriate autonomy and supported the use of "authorized deception." She said researchers who use deception should be required to demonstrate the following:

- The research addresses nontrivial question and is validly designed.
- The researcher has the skill and resources to minimize participants' upset.
- The debriefing leaves subject knowledgeable and satisfied.
- A procedure such as the "Reactions to Research Participation Questionnaire (RRPQ) will be employed after each trial to ensure that no harm is occurring.
- Some form of consent will be employed.

DISCUSSION

Several SACHRP members expressed appreciation for the helpful overview of the nature of the problem.

"Valid consent." Dr. Ross observed that Dr. Miller used the term "valid consent," which is not regulatory language. Dr. Miller responded that consent must be valid from a moral standpoint, and his use of the term reflects this principle.

Offer to withdraw. Dr. Ross asked Dr. Miller to elaborate on the idea that the debriefing should include an offer to withdraw, noting that this might lead to invalid data. He responded that the very requirement for informed consent is a potentially biasing factor. If a large number of people withdrew upon being debriefed, however, there might be a need to rethink the approach.

Dr. Strauss said that his institution has relied on the American Psychological Society for guidance on deceptive research. The IRB struggles with the issue, however. Operationalizing an ethical approach might mean being able to say that the researcher does not believe the information being withheld is likely to cause the subject not to wish to participate. Dr. Miller observed that insofar as this can be known, it is a strong reason not to do a study if you think the information being withheld is likely to cause subjects to withdraw.

Gathering data. Dr. Strauss continued, noting that IRBs struggle to discern foreseeable risks, but cannot always know the impact a study might have. He felt that IRBs should be obligated to ask investigators for feedback from subjects on actual experiences to inform their decisions (for example, participants in a study in which people were accepted or rejected by people they thought were prospective dates). He was interested in using brain imaging as one source of feedback. Dr. Ross endorsed the idea of gathering data.

Similarity to placebo trials. Mr. Forster observed that the language Dr. Miller suggested for debriefing seemed similar to language that might be used in a briefing for a placebo trial. The speaker said it was analogous. If nothing were being withheld about the study, it would be the same; however, in deception research, subjects are consenting to things they will not know about until after participating.

Adverse consequences. Dr. Ross wondered how responsible researchers would feel about the possibility of adverse consequences – even, for some involved in the Milgram study, PTSD. Dr. Sieber said it was important to consider separately the aftereffects of the study and how subjects feel about misperceiving their own actions. There can be value in "inflicted insight," and people can even be grateful for what they learned.

However, adverse consequences do need to be thought through carefully. She suggested you may tell subjects what they are likely to experience, which is different from revealing the research strategy. For example, you can say, "you might find yourself doing something you don't want to do." A small percentage of people will say, "I don't want to do this."

Dr. Strauss expressed a number of reservations about research involving deception and the AD approach, noting that research involving college students typically make little effort to exclude anyone and that subjects may lack the self-perception needed to know when to exclude themselves. He also observed that there are ethical dilemmas involved in participant observation studies in which the researcher is embedded in a situation, such as a chatline. Do these situations make it tougher for researchers trying to build trust with potential subjects?

Dr. Ross accepted the critique, adding that anyone who wants to lurk in a chatroom or participate as a member /researcher has a serious obligation to make themselves known to the leader of the group and determine what kind of informed consent is best. For example, participating in a group of people who are victims of violence could make them feel unsafe; if this is the case, research should not proceed.

Dr. Marshall agreed with Dr. Strauss about the inability of potential participants to be good judges about the impact of a psychology experiment on their emotions. People tend not to know. She commented that in some ethnographic and epidemiological studies, such as a study of injection drug users, team members have used a guide who provided an introduction to the setting. The person running the gallery knew about the researchers' presence. Dr. Ross reinforced the approach, stressing the importance of making sure the leader of a session that is

being observed is aware of and approves the researcher's presence. This should be coupled with assurance of anonymity for subjects. Dr. Marshall added, however, that it is often not clear who the "leader" is. Dr. Strauss commented that some studies involving deception may be classified as more than minimal risk.

Guidance and sharing. Mr. Forster asked the OHRP Director if the types of situations discussed above were worth of guidance. Dr. Menikoff responded, "maybe."

Dr. Bierer commended the practical and useful approaches presented by the speakers. She felt it would be a contribution to share them with the research community.

Focus on Data Identifiability

- ***Sara C. Hull, Ph.D.,*** *Director, NHGRI Bioethics Core; Faculty, NIH Clinical Center Department of Bioethics*
- ***David W. Craig, Ph.D.,*** *Associate Director & Investigator, Neurogenomics Division, The Translational Genomics Research Institute*
- ***Bradley Malin, Ph.D.*** *Assistant Professor, Department of Biomedical Informatics, School of Medicine, Vanderbilt University*
- ***Jane Kaye, D. Phil****., Director, HeLEX, Centre for Health, Law and Emerging Technologies Department of Public Health, University of Oxford*

Remarks by Sara C. Hull: Identifiability: A Useful or Decrepit Concept in Research Ethics?

Dr. Hull observed that oversight of research is based on assumptions about informational privacy that may no longer apply to "deidentified" material in data bases. A current debate in the field of bioethics centers on whether deidentification is sufficient to protect health privacy in research, given advances in the use of computer technology that make it possible to identify probable subjects based on minimal information. Significantly fewer studies now require IRB review, leaving a growing gap in human subject protection. Dr. Hull called for the evaluation of newly created oversight and governance structures to assess their effectiveness at addressing issues related to identifiability in data bases.

Remarks by David W. Craig: Resolving Membership in a Study in Shared Aggregate Genetics Data

Dr. Craig explained that de novo changes in genomes make it increasingly possible to determine whether or not a particular individual participated in a study. Yet, multiple studies available on the Web list every single nucleotide polymorphisms, or SNPs (pronounced "snips"). (A SNP is a DNA sequence variation that occurs when a single nucleotide in the genome sequence is altered.) Once as many as 1000 SNPs are included in an aggregate data set, it is relatively easy to identify specific individuals. Recognizing this capability, NIH no longer makes summary-level data from genome studies freely available on the Web. Dr. Craig and others are working with NIH to develop guidance for measuring the risk of identifiability for particular data sets.

The speaker cautioned that the "era of whole-genome sequencing is approaching." In addition to the issue of identifiability for individuals, we must also face the possibility that descendants and

relatives might learn about family risks for diseases such as Alzheimer's as a result of an individual's participation, or that this risk might be revealed to other parties. The use of DNA post-mortem adds an additional wrinkle in the calculation of potential risk.

Remarks by Bradley Malin: Measuring Identifiability from a "Reasonable" View

Dr. Malin observed that it takes few features to make an individual unique. Strikingly, the 5-digit zip code, birthdate, and gender are sufficient data points to identify 63-87 percent of persons in the U.S. The HIPAA Safe Harbor principles require the removal of 18 attributes and prohibit the disclosure of geocodes if there are less than 20,000 people in an area (see http://www.hhs.gov/ocr/privacy/hipaa/understanding/summary/index.html); however, a Limited Dataset can retain dates and geocodes. Nearly one-third of residents in many states reside in a geocode inhabited by 20,000 persons or less.

Dr. Malin argued, however, that being able to "distinguish" an individual is not the same as being able to "identify" that individual. He notes that if a person had deidentified DNA but no way to link this information to an individual, privacy would still be maintained. Voter registration data, for example, are generally insufficient to identify individuals. He added that researchers in a recent study at the University of Chicago reviewed a dataset containing 15,000 records stored according to Safe Harbor principles and could only identify two specific individuals.

The speaker closed with the recommendation that, while it takes time and energy to appropriately model risks, we can and should do it. Risks are data dependent and require expert guidance to assess the risks of identifying individuals in a particular data set. He proposed the creation of a national center that can offer guidance on how to assess these risks.

Remarks by Jane Kaye: Protecting Participants in a Global Research Community

Dr. Kaye put the issue of identifiable data in a global context. She noted that while the United Kingdom has focused considerable effort on making data unidentifiable so it can be used for multiple research purposes without asking participants for consent, in some instances we really need large repositories of data in which you *can* go back to individuals in some circumstances.

Technological advances make it possible for computers to interrogate data, and next generation sequencing adds additional capabilities. New scientific questions can be asked in studies that may literally involve millions of people represented in biobanks. These trends test the basic principles of medical research, including informed consent, the right to withdraw from research, and the social contract that assures research participants that their private information will remain confidential.

The speaker asserted that we can no longer promise subjects that personal information will remain confidential. DNA is a unique identifier. Data can be replicated indefinitely, shared globally, and linked to other datasets. At the same time, the increased quantity of data available on individuals increases the likelihood of identifying serious treatable conditions and incidental findings. This raises the issue of whether researchers are obligated to provide feedback and, if so, whether secondary and tertiary researchers should be held responsible for doing so.

The speaker called for new forms of governance that feature "participant-centric" approaches, offering people greater control over the use of their information if they so desire. She envisioned decreasing reliance on research ethics committees to represent the concerns of participants.

Rather, the preferred model may become ongoing dialogue with representative participants who become partners in the research process.

DISCUSSION

Dr. Bierer observed that presentations touched on the issue that much data collection is done outside of Federal oversight and is outside the purview of SACHRP. She added that it would be a fallacy to assume that most institutions have established data use committees or similar controls. She asked speakers to suggest next steps for SACHRP. They responded:

- Dr. Craig suggested guidance that acknowledges "shades of grey" and does not prevent data sharing.
- Dr. Kaye said that individuals who are concerned about confidentiality are not always aware of the issue of identifiability.
- Dr. Hull agreed that shades of grey must be acknowledged and added that research subjects have a variety of views on privacy issues. Some are primarily concerned with allowing research to go forward that may give them a chance at better quality of life.
- Dr. Malin pointed to the need to clarify the objective. What are we really trying to accomplish in this area?

Dr. Goldkind observed that there is a good deal we don't know at present about public perceptions of the use of data, especially biospecimens. Dr. Hull suggested involving individuals who represent subjects in the governance of resources such as biobanks. Dr. Marshall agreed that this is an appropriate approach. Some models also involve the use of random calls to subjects to address issues that arise. Dr. Malin pointed out the danger of contacting people too frequently, explaining that they may stop listening.

Dr. Strauss stated that our ability to guide ethical considerations related to technology is limited; the pace of technology has far outpaced our thinking. Once data are de-identified, regulatory controls are inadequate. A firm guideline, however, is that data use should adhere to the terms of the original consent.

Dr. Gibbons asked the panel to comment on the possibility of bidirectional communication rather than one-time consent. He was also interested in ways to communicate beneficial findings to participants. Dr. Kaye said she would like to see this happen, but models are still being worked out. Dr. Malin said that Vanderbilt does not return results; in fact, investigators sign documents saying they will not recontact participants. Dr. Craig added that sharing results with subjects is appropriate only if they have been validated.

Mr. Forster said that group reviews, structural methods such as contracts, and intensive community engagement have been used to approach these issues. He asked about other models. Dr. Malin said that models vary depending on the context; for example, regulations come into play for entities covered under HIPAA. There are market-based models in which the information brokerage houses act on behalf of a business or agency. Dr. Hull said that in addition to HIPAA, the Genetic Information Nondiscrimination Act must be considered.

Dr. Bledsoe asked speakers to comment on the need for broad public education on the issues discussed. Dr. Craig said the public needs to know that there is always a risk of identifiability. He agreed that it was important to educate the community on how to assess and quantify risk. Dr.

Kaye felt that government should devise a broad strategy to do this. Dr. Malin observed, however, that there is a challenge in determining who to educate; further, deidentification means different things to different people. He said he had not seen good examples of what can go wrong, though acknowledged these may not be publicly reported

Dr. Marshall pointed to a great need for public education on genetic research, its potential, and limitations. She felt that this should be addressed through private and public partnerships in which participants, donors, researchers, and providers (among others) are involved. Appropriate participants would depend on the local context and the specific issues being addressed.

The Chair thanked the panel for an "enlightening, directional, challenging presentation.

Public Comment

Public comment was invited, but no comments were offered. The Chair closed the meeting.

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Attachment A.
Letter Regarding NPRM on Modifications to HIPAA Rules (As Presented)

October 10, 2010

Re: Modifications to the HIPAA Privacy, Security, and Enforcement Rules Under the Health Information Technology for Economic and Clinical Health Act; Proposed Rule

Dear :

The Secretary's Advisory Committee on Human Research Protections (SACHRP) advises the Secretary of the U.S. Department of Health and Human Services (HHS) on human subjects research protection issues. Shortly after its creation in 2003, SACHRP began developing recommendations on significant topics in research, with one of the earliest themes being privacy protection and regulation. It is within that historical context -- and in recognition of current expanded abilities to access identifiable data and materials -- that SACHRP, by this letter, offers its comments on the HHS Notice of Proposed Rulemaking that modifies the Privacy and Security Rules in light of the Health Information Technology for Economic and Clinical Health Act (HITECH).[1]

In September 2004, SACHRP submitted several recommendations to the Secretary to address the Privacy Rule issued under the Health Insurance Portability and Accountability Act (HIPAA). A recurrent theme in the recommendations was the need for more coordination and less complexity among HHS requirements for human subjects research, including HIPAA privacy requirements. As SACHRP explained at the time:

> … SACHRP appreciates the fact that human subjects research is, in the regulatory sense, a complicated endeavor, often under the concurrent jurisdiction of the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA) and other agencies. The accretions of years of guidance from these agencies must be coordinated with the complexities of the new HIPAA requirements…. As set forth in this letter, SACHRP is concerned that in some areas, the application of HIPAA to human subjects research has unnecessarily complicated research activities, including IRB review and oversight.

SACHRP Chair Letter to HHS Secretary on HIPAA, September 27, 2004, *available at* http://www.hhs.gov/ohrp/sachrp/hipaalettertosecy090104.html [hereinafter SACHRP Chair Letter, September 27, 2004].

[1] 75 Fed. Reg. 40868 (July 14, 2010).

In this letter, we reiterate the importance of a harmonized approach within HHS to human subjects research regulation, including privacy regulation that now includes HIPAA and HITECH. More specifically, we address several research-specific issues in the NPRM – including compound authorizations, future research, the "minimum necessary" standard, business associates, and restrictions on the sale of protected health information (PHI) – and do so primarily in the context of SACHRP's prior recommendations for harmonization on these topics.

I. Compound Authorizations (75 FR 40892-93)

HIPAA generally prohibits the use of a "compound authorization," which is a HIPAA authorization that is combined with another type of legal permission. One exception is that a research consent form and HIPAA authorization can be combined in clinical trials. However, HHS previously took the position that if a clinical trial also included specimen/data banking, then a separate authorization for banking was needed because the "banking" activity must be regarded as distinct from the clinical trial.

In SACHRP's 2004 recommendations, it expressed concern that HHS's rule on compound authorizations overcomplicated banking research and revealed a lack of harmonization with OHRP, which allowed one consent form for a clinical trial that had a banking component. As SACHRP proposed:

> **Recommendation V**: The Department should revise HIPAA's compound authorization rules to permit the combining of research authorizations into one form when researchers seek to bank data and materials collected as part of an underlying clinical trial; however, in order to promote patients/subject choice, the rules should require that subjects be given the ability to "opt in" to the banking portion of the authorization. (Refer to Appendix E).[2]

SACHRP Chair Letter, September 27, 2004 (emphasis added).

SACHRP appreciates HHS's recognition of this recommendation in the NPRM. HHS cites Recommendation V above for its new proposal to allow one combined authorization for a clinical trial that also includes banking, as long as covered entities distinguish between which activity is "conditioned" on signing the authorization (i.e., the clinical trial) and which activity is optional or "unconditioned" (i.e., banking).[3] HHS appropriately acknowledges that "multiple

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[2] Appendix E explained in part: "While SACHRP recognizes the distinct importance of the informed consent and HIPAA authorization documents and appreciates the Department's clarifications regarding combining research informed consents with HIPAA research authorization forms, the more integrated the information provided to subjects, whether required by the Common Rule or the Privacy Rule, the better chance that the resulting consent and authorization will be meaningful to subjects." SACHRP Chair Letter, September 27, 2004, Appendix E, *available at* http://www.hhs.gov/ohrp/sachrp/appendixe.html.

[3] 75 Fed. Reg. at 40893.

forms may be confusing for research subjects," "documenting and storing twice as many authorizations is a major concern," and reportedly, "recruitment into clinical trials has been hampered, in part, because [of] the multiplicity of forms."[4]

We offer the following comments:

1. SACHRP supports HHS's proposal to modify the Privacy Rule to allow a covered entity to use one consolidated authorization that covers a clinical trial and a banking component. In particular, we support the harmonization goal of this proposal, as it would better align HIPAA with Common Rule informed consent requirements, as interpreted by OHRP.

2. We request that HHS confirm in the final rule, for the sake of clarity in application, that compound authorizations are permissible for any type of combined research studies, including but not limited to clinical trials with a banking component (provided that the conditioned and unconditioned activities are clear). For example, we believe HHS's proposal would allow a covered entity to use a combined authorization for (i) a clinical trial and optional sub-study or sub-studies (*e.g.*, a pharmacokinetic sub-study using data from a clinical trial), and (ii) a banking protocol that permits secondary research.

3. We support HHS's proposal to give covered entities flexibility in how to distinguish between conditioned and unconditioned activities in their forms. For example, HHS notes that a check-box or extra page explaining the "unconditioned" (banking) activity may be appropriate. We ask that HHS encourage entities to implement the new standard in a way that minimizes duplicative or confusing information for potential research participants. We also recommend that HHS allow entities to present the "unconditioned" activity in ways that can be most easily tracked. This would help to ensure that entities are able to honor individuals' requests and avoid negative effects on individuals' interests. To illustrate these points, SACHRP offers three models in Attachment A that we believe should be acceptable under the final rule and ask that HHS confirm their acceptability.

4. We ask HHS to confirm that its proposal does not affect the availability of the waiver provisions in the existing Privacy Rule. That is, if a covered entity uses a compound authorization for a clinical trial with a banking component, and a researcher later proposes to an IRB or a Privacy Board a new study that is distinct from both the original study and the banking activity, the covered entity, through its IRB or Privacy Board, may consider and approve a waiver of authorization to allow the third, new study to be undertaken.

5. We recommend that HHS clarify the effect of revoking only <u>one</u> part of a compound authorization. For example, if a covered entity uses a combined consent/authorization for a clinical trial and optional banking research, and an individual

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who authorized all the research later revokes authorization for banking, then the covered entity may still rely on the consent/authorization for the clinical trial.

6. We encourage HHS to engage in ongoing dialogue with covered entities to develop best practices for documentation that satisfy the new proposed compound authorization rule. The harmonization goal is best achieved if entities can satisfy HIPAA, Common Rule, and FDA requirements with one template form.

7. We ask HHS to clarify the practical implications of a finalized compound authorization rule for covered entities, in terms of the timing of compliance and permissible strategies for new studies and previously approved, ongoing studies.

II. Future/Secondary Research (75 FR 40893-94)

HHS previously took the position that an authorization must be study-specific and could not authorize broad areas of future/secondary research. This interpretation conflicted with OHRP's view that informed consent may describe both a specific study and the possibility of future/secondary research. As SACHRP explained in 2004:

> **Recommendation IV:** When an IRB has considered and approved a research consent form that permits consent to certain future uses under the Common Rule standard, the Final Privacy Rule should likewise permit subjects to authorize the use and disclosure of their PHI for the same future uses. Any subsequent research using the PHI that goes beyond the scope of the authorization to future uses or disclosures would require IRB or Privacy Board waiver of the Privacy Rule's Authorization requirements, or subsequent authorization from each subject. (Refer to Appendix D).

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SACHRP appreciates HHS's recognition of this recommendation in the NPRM. HHS cites Recommendation IV above for its proposed new interpretation that would allow an authorization for future/secondary research. We support the harmonization goal of this proposal, and believe that this proposal for the HIPAA authorization is more consistent with OHRP's interpretation of Common Rule informed consent requirements.

HHS requested comment on what degree of specificity the Privacy Rule should require in an authorization for future research. We support an approach that best meets harmonization goals so that covered entities can use a consistent approach to obtaining informed consent for future research and authorization for the same scope of future research.

SACHRP offers the following comments:

1. We believe that an informed consent and authorization, together, should provide appropriate information such that it would be reasonable for an individual to expect that his/her health information could be used or disclosed for the research. Consistent with informed

consent standards, the authorization should be reasonably specific such that individuals are aware of the types of research that may be conducted. IRBs are already responsible under the Common Rule for determining what information is material to potential participants before they agree to research, including future/secondary research. We do not recommend requiring IRBs or covered entities to adopt prescribed statements about certain types of research, because conceptions of the types of research requiring special considerations, such as "sensitive" research, change over time. In addition, IRBs need flexibility in approving consent forms to address concerns unique to particular subject populations, and prescribed authorization statements may conflict with an IRB's judgments about how to describe the research appropriately in the informed consent.

2. We recommend that HHS clarify in the final rule that covered entities have flexibility in applying the existing authorization elements (45 CFR 164.508) to future/secondary research. The existing elements are designed to apply to a specific research activity and are, or could be interpreted to be, too rigid for future/secondary research. Examples include:

- The existing authorization standards require a revocation to be in writing. For longer-term research studies, such as banking research and future/secondary research, HHS should permit (but not require) covered entities to accept an oral revocation by an individual (such as by telephone call to the researcher or institution), as this is less burdensome to individuals. [45 CFR 164.508(b)(5) and (c)(2)(i).]

- An authorization currently must identify the health information to be used or disclosed in a "specific and meaningful fashion." For future/secondary research, a high level of specificity may not be possible. Covered entities should be allowed to describe the information reasonably, consistent with the nature of research described in the authorization. For example, if updated medical information (beyond the information collected at the time of the original study) may be used for the future research, statements such as "your future medical records [at Hospital]" or "your future medical records [relating to diseases/conditions]" should be regarded as satisfying the standard. We request this clarification because some biobanks enrich the research value of stored specimens through ongoing linkage to medical information (*e.g.*, outcomes data), so covered entities will need to know if statements such as the above appropriately inform individuals under the Privacy Rule. [45 CFR 164.508(c)(1)(i).]

- An authorization currently must be specific as to the "person(s), or class of persons, to whom the covered entity may make the requested use or disclosure." The level of specificity for this standard should be reasonably interpreted and flexibility should be allowed, in light of the uncertainty of the identity of future researchers who will have legitimate research need to access the PHI. For example, it would be helpful if HHS could accept the proposition that "other researchers at academic or commercial entities domestically or outside the U.S." is permissible, in the interests of ensuring individuals are aware upfront of the potential breadth of disclosures; such an expression of the identity of future researchers is already often allowed by IRBs in approving consent forms for future, "downstream" research. An alternative is that

covered entities would need to specify a group initially (e.g., "other oncology researchers"), but may need, through IRBs or privacy boards, to consider waiving authorization downstream for a different disclosure. [45 CFR 164.508(c)(1)(iii).]

3. In the interests of harmonization, we request that OCR and OHRP consult with FDA to determine whether a consent/authorization to future/secondary research that meets Common Rule and Privacy Rule standards also meets FDA standards for informed consent. It would be most useful and efficient if these three offices within HHS could adopt a common approach to this issue.

4. We recommend that HHS grandfather existing, ongoing studies that involve the possibility of future/secondary research, if an IRB-approved consent reasonably informed the individuals of how their health information could be used or shared for such research.

5. We ask HHS to clarify the practical implications for covered entities of the new interpretation that would allow authorizations for future/secondary research, including the timing of compliance and permissible approaches for new studies.

III. Minimum Necessary (75 FR 40896)

HHS requested input as it develops required guidance under HITECH on the "minimum necessary" standard. SACHRP supports the flexibility permitted under the minimum necessary standard in the original Privacy Rule, as that standard applies to research. The standard and its interpretation should not be changed in any way that affects IRBs, or that affects covered entities' ability to rely on a researcher's representation as to the minimum necessary information needed for a research use.

IV. Business Associates (75 FR 40872-74)

HITECH substantially expands the requirements and the liability of business associates. Existing HHS guidance clarifies that researchers generally are not business associates because research is not a "covered function." SACHRP requests that HHS confirm that outsourced research review, approval, and continuing oversight functions (such as through using an external or independent IRB) similarly do not give rise to a business associate relationship. This clarification would serve an important harmonization goal, as federal policy looks increasingly toward the use of central IRBs (which are outside of and separate from a covered entity's own IRB). We are concerned that if outside IRBs were regarded as business associates, this could deter some entities from using them, as the need to negotiate business associate agreements and related liability risks under HITECH would be a new, time- and resource-intensive requirement for IRBs and the institutions that they serve. Any such disincentive to use external, central IRBs would undermine and run contrary to the position of, for example, the NIH, which increasingly has supported the use of central IRBs in multi-site studies.

V. No Sale of PHI (75 FR 40890-92)

HITECH prohibits a covered entity or business associate from receiving direct or indirect remuneration in exchange for the disclosure of protected health information, without individual

authorization. The research exception permits a covered entity to receive a reasonable, cost-based fee to cover the cost of preparing and transmitting information for research purposes. We ask that HHS clarify how this provision applies to a scenario in which a covered entity discloses protected health information to a business associate for one purpose (*e.g.*, quality benchmarking), and the business associate asserts the right to create a limited data set and use or disclose it for separate, unrelated research by itself or other third parties.

- For example, the business associate may aggregate identifiable information that it receives for benchmarking purposes in its own proprietary database, and then make a limited data set available to other parties for research, for a fee. We ask that HHS clarify whether this is impermissible direct or indirect remuneration to the business associate (which already has been paid for the primary service), unless the covered entity obtains individuals' written authorization.

We appreciate the careful attention that SACHRP's prior recommendations have received. Thank you for the opportunity to comment.

Sincerely,

[Chair, SACHRP]

ATTACHMENT A: MODELS OF COMPOUND AUTHORIZATION

FOR A CLINICAL TRIAL & BANKING COMPONENT

Model 1: Combined consent/authorization for clinical trial and banking component, with check-boxes for banking option, and one signature

The covered entity uses a combined consent/authorization, in which the authorization elements for the optional banking activity "piggyback" on authorization statements for the clinical trial. In other words, the recitation of authorization elements is not entirely separate for the banking component, but relevant differences for banking authorization are noted. Through check-boxes, an individual is asked for consent and authorization for the clinical trial and for the optional banking research. A single signature would be provided.

For an example, please see the mark-ups to the Authorization on the next page. This Authorization is the sample published in the NIH/OCR guidance entitled "HIPAA Authorization for Research," available at http://privacyruleandresearch.nih.gov/pdf/authorization.pdf. Mark-ups are shown in **bold red CAPS**.

Model 2: Combined consent/authorization form for clinical trial and banking component, with one signature for clinical trial and another signature for banking

The covered entity uses a combined consent/authorization, in which the authorization has two sections: one for the clinical trial, and one for the optional banking research (*e.g.*, in a separate paragraph or section). An individual is asked for consent and authorization for the clinical trial and the optional banking research. Separate signatures are requested.

Model 3: Combined consent/authorization form for clinical trial and banking component, with check boxes for banking option, but with detailed information about banking presented in a separate brochure or information sheet

The covered entity uses a combined consent/authorization form for a clinical trial with an optional banking component. As part of the IRB-approved informed consent process, the covered entity gives individuals an informational brochure that describes banking research, including in part whether identifiable health information will be used or shared and for what purposes. The consent/authorization, together with the informational brochure, meaningfully inform individuals of the banking option. An individual is asked for consent/authorization to the clinical trial and optional banking component. A single signature would be provided.

SAMPLE AUTHORIZATION LANGUAGE FOR RESEARCH USES AND DISCLOSURES OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION BY A COVERED HEALTH CARE PROVIDER

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study AND OPTIONAL BANKING STUDY

REQUIRED ELEMENTS:

If you sign this document, you give permission to [name or other identification of specific health care provider(s) or description of classes of persons, e.g., all doctors, all health care providers] at [name of covered entity or entities] to use or disclose (release) your health information that identifies you for the research study described below:

[Provide a description of the research study, such as the title and purpose of the research.][ADD OPTIONAL BANKING STUDY]

The health information that we may use or disclose (release) for this research includes [complete as appropriate]:

[Provide a description of information to be used or disclosed for the research project. This may include, for example, all information in a medical record, results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.][STATE WHETHER INFORMATION IS THE SAME OR DIFFERENT FOR THE OPTIONAL COMPONENT]

The health information listed above may be used by and/or disclosed (released) to:

[Name or class of persons involved in the research; i.e., researchers and their staff]

[*Footnote to the Template provides additional examples of who may have access to PHI for the study, including but not limited to research collaborators, sponsors, data coordinating centers, IRBs, Data Safety and Monitoring Boards, and any other entity [or governmental party] to whom the covered entity is expected to make the disclosure.]*

[FOR THE BANKING COMPONENT, INCLUDE WHO MAY USE PHI AND TO WHOM PHI MAY BE DISCLOSED]

[Name of covered entity] is required by law to protect your health information. By signing this document, you authorize [name of covered entity] to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. Please note that [include the appropriate statement]:

- You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment **IN THE CLINICAL TRIAL.**
  (When the research involves treatment and is conducted by the covered entity or

when the covered entity provides health care solely for the purpose of creating protected health information to disclose to a researcher)

- **IF YOU WANT TO ALLOW YOUR HEALTH INFORMATION TO BE USED OR SHARED FOR THE OPTIONAL BANKING RESEARCH, THEN PLEASE SELECT THE CHOICE BELOW THAT INCLUDES BANKING. IF YOU DO NOT AUTHORIZE THE BANKING RESEARCH, YOU MAY STILL PARTICIPATE IN THE CLINICAL TRIAL.**

- [Name of covered entity] may not condition (withhold or refuse) treating you on whether you sign this Authorization.
  (When the research does <u>not</u> involve research-related treatment by the covered entity or when the covered entity is <u>not</u> providing health care solely for the purpose of creating protected health information to disclose to a researcher)

Please note that [include the appropriate statement]

- You may change your mind and revoke (take back) this Authorization at any time, except to the extent that [name of covered entity(ies)] has already acted based on this Authorization. To revoke this Authorization, you must write to: [name of the covered entity(ies) and contact information].
  (Where the research study is conducted by an entity other than the covered entity)
- You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, [name or class of persons at the covered entity involved in the research] may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to: [name of the covered entity(ies) and contact information].
  (Where the research study is conducted by the covered entity)

  [FOR BANKING COMPONENT, ADD CONTACTS IF DIFFERENT]

- **IF YOU AUTHORIZE YOUR HEALTH INFORMATION TO BE USED AND SHARED FOR BOTH THE CLINICAL TRIAL AND BANKING, AND LATER REVOKE YOUR AUTHORIZATION FOR ONLY ONE OF THESE ACTIVITIES, THIS AUTHORIZATION WILL REMAIN IN EFFECT FOR THE OTHER ACTIVITY**.

This Authorization does not have an expiration date [or as appropriate, insert expiration date or event, such as "end of the research study."] **[ADDRESS WHETHER EXPIRATION DIFFERS FOR BANKING COMPONENT]**

[ADD CHECK-BOXES OR OTHER MEANS TO CLARIFY WHETHER INDIVIDUAL IS AUTHORIZING THE CLINICAL TRIAL AND BANKING, OR ONLY THE CLINICAL TRIAL]

_____

Signature of participant or participant’s personal representative

_____

Printed name of participant or participant’s personal representative

_____

Date

_____

If applicable, a description of the personal representative’s authority to sign for the participant.

Attachment B.
Final Letter Regarding NPRM on Modifications to HIPAA Rules (As Approved)

October 10, 2010

Re: Modifications to the HIPAA Privacy, Security, and Enforcement Rules Under the Health Information Technology for Economic and Clinical Health Act; Proposed Rule

Dear : :

The Secretary's Advisory Committee on Human Research Protections (SACHRP) advises the Secretary of the U.S. Department of Health and Human Services (HHS) on human subjects research protection issues. Shortly after its creation in 2003, SACHRP began developing recommendations on significant topics in research, with one of the earliest themes being privacy protection and regulation. It is within that historical context -- and in recognition of current expanded abilities to access identifiable data and materials -- that SACHRP, by this letter, offers its comments on the HHS Notice of Proposed Rulemaking that modifies the Privacy and Security Rules in light of the Health Information Technology for Economic and Clinical Health Act (HITECH).[5]

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> … SACHRP appreciates the fact that human subjects research is, in the regulatory sense, a complicated endeavor, often under the concurrent jurisdiction of the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA) and other agencies. The accretions of years of guidance from these agencies must be coordinated with the complexities of the new HIPAA requirements…. As set forth in this letter, SACHRP is concerned that in some areas, the application of HIPAA to human subjects research has unnecessarily complicated research activities, including IRB review and oversight.

[5] 75 Fed. Reg. 40868 (July 14, 2010).

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In this letter, we reiterate the importance of a harmonized approach within HHS to human subjects research regulation, including privacy regulation that now includes HIPAA and HITECH. More specifically, we address several research-specific issues in the NPRM – including compound authorizations, future research, the "minimum necessary" standard, business associates, and restrictions on the sale of protected health information (PHI) – and do so primarily in the context of SACHRP's prior recommendations for harmonization on these topics.

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> **Recommendation V**: The Department should revise HIPAA's compound authorization rules to permit the combining of research authorizations into one form when researchers seek to bank data and materials collected as part of an underlying clinical trial; however, in order to promote patients/subject choice, the rules should require that subjects be given the ability to "opt in" to the banking portion of the authorization. (Refer to Appendix E).[6]

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clinical trial that also includes banking, as long as covered entities distinguish between which activity is "conditioned" on signing the authorization (i.e., the clinical trial) and which activity is optional or "unconditioned" (i.e., banking).[7] HHS appropriately acknowledges that "multiple forms may be confusing for research subjects," "documenting and storing twice as many authorizations is a major concern," and reportedly, "recruitment into clinical trials has been hampered, in part, because [of] the multiplicity of forms."[8]

We offer the following comments:

1. SACHRP supports HHS's proposal to modify the Privacy Rule to allow a covered entity to use one consolidated authorization that covers a clinical trial and a banking component. In particular, we support the harmonization goal of this proposal, as it would better align HIPAA with Common Rule informed consent requirements, as interpreted by OHRP.

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Board, may consider and approve a waiver of authorization to allow the third, new study to be undertaken.

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and believe that this proposal for the HIPAA authorization is more consistent with OHRP's interpretation of Common Rule informed consent requirements.

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- The existing authorization standards require a revocation to be in writing. For longer-term research studies, such as banking research and future/secondary research, HHS should permit (but not require) covered entities to accept an oral revocation by an individual (such as by telephone call to the researcher or institution), as this is less burdensome to individuals. [45 CFR 164.508(b)(5) and (c)(2)(i).]

- An authorization currently must identify the health information to be used or disclosed in a "specific and meaningful fashion." For future/secondary research, a high level of specificity may not be possible. Covered entities should be allowed to describe the information reasonably, consistent with the nature of research described in the authorization. For example, if updated medical information (beyond the information collected at the time of the original study) may be used for the future

research, statements such as "your future medical records [at Hospital]" or "your future medical records [relating to diseases/conditions]" should be regarded as satisfying the standard. We request this clarification because some biobanks enrich the research value of stored specimens through ongoing linkage to medical information (*e.g.*, outcomes data), so covered entities will need to know if statements such as the above appropriately inform individuals under the Privacy Rule. [45 CFR 164.508(c)(1)(i).]

- An authorization currently must be specific as to the "person(s), or class of persons, to whom the covered entity may make the requested use or disclosure." The level of specificity for this standard should be reasonably interpreted and flexibility should be allowed, in light of the uncertainty of the identity of future researchers who will have legitimate research need to access the PHI. For example, it would be helpful if HHS could accept the proposition that "other researchers at academic or commercial entities domestically or outside the U.S." is permissible, in the interests of ensuring individuals are aware upfront of the potential breadth of disclosures; such an expression of the identity of future researchers is already often allowed by IRBs in approving consent forms for future, "downstream" research. An alternative is that covered entities would need to specify a group initially (e.g., "other oncology researchers"), but may need, through IRBs or privacy boards, to consider waiving authorization downstream for a different disclosure. [45 CFR 164.508(c)(1)(iii).]

3. In the interests of harmonization, we request that OCR and OHRP consult with FDA to determine whether a consent/authorization to future/secondary research that meets Common Rule and Privacy Rule standards also meets FDA standards for informed consent. It would be most useful and efficient if these three offices within HHS could adopt a common approach to this issue.

4. We recommend that HHS grandfather existing, ongoing studies that involve the possibility of future/secondary research, if an IRB-approved consent reasonably informed the individuals of how their health information could be used or shared for such research.

5. We ask HHS to clarify the practical implications for covered entities of the new interpretation that would allow authorizations for future/secondary research, including the timing of compliance and permissible approaches for new studies.

III. Minimum Necessary (75 FR 40896)

HHS requested input as it develops required guidance under HITECH on the "minimum necessary" standard. SACHRP supports the flexibility permitted under the minimum necessary standard in the original Privacy Rule, as that standard applies to research. The standard and its interpretation should not be changed in any way that affects IRBs, or that affects covered

entities' ability to rely on a researcher's representation as to the minimum necessary information needed for a research use.

IV. Business Associates (75 FR 40872-74)

HITECH substantially expands the requirements and the liability of business associates. Existing HHS guidance clarifies that researchers generally are not business associates because research is not a "covered function." SACHRP requests that HHS confirm that outsourced research review, approval, and continuing oversight functions (such as through using an external or independent IRB) similarly do not give rise to a business associate relationship. This clarification would serve an important harmonization goal, as federal policy looks increasingly toward the use of central IRBs (which are outside of and separate from a covered entity's own IRB). We are concerned that if outside IRBs were regarded as business associates, this could deter some entities from using them, as the need to negotiate business associate agreements and related liability risks under HITECH would be a new, time- and resource-intensive requirement for IRBs and the institutions that they serve. Any such disincentive to use external, central IRBs would undermine and run contrary to the position of, for example, the NIH, which increasingly has supported the use of central IRBs in multi-site studies.

V. No Sale of PHI (75 FR 40890-92)

HITECH prohibits a covered entity or business associate from receiving direct or indirect remuneration in exchange for the disclosure of protected health information, without individual authorization. The research exception permits a covered entity to receive a reasonable, cost-based fee to cover the cost of preparing and transmitting information for research purposes. We ask that HHS clarify how this provision applies to a scenario in which a covered entity discloses protected health information to a business associate for one purpose (*e.g.*, quality benchmarking), and the business associate asserts the right to create a limited data set and use or disclose it for separate, unrelated research by itself or other third parties.

- For example, the business associate may aggregate identifiable information that it receives for benchmarking purposes in its own proprietary database, and then make a limited data set available to other parties for research, for a fee. We ask that HHS clarify whether this is impermissible direct or indirect remuneration to the business associate (which already has been paid for the primary service), unless the covered entity obtains individuals' written authorization.
- **A pharmaceutical or device company funds a researcher within a hospital to perform (under a waiver of consent and authorization) a retrospective records review study of patient records within that hospital, to determine adverse effects, if any, of a drug or device. We ask OCR to confirm that, unless authorizations**

are obtained, the covered entity hospital may accept only a reasonable fee that covers the study and its assembling and transmittal of the data.

- **Alternately, the company may offer to pay the medical records department or QA office of the hospital to assemble these data, under a waiver of authorization and consent granted by the hospital's IRB/privacy board to a company researcher. In this scenario, the assembling of the data is done by the medical records department or QA office, and is transmitted to the company. We ask OCR to confirm that the hospital may accept only a reasonable fee for this service, including transmittal of the data.**
- **A pharmaceutical or device company sponsor pays a covered entity for carrying out a clinical trial. As part of the trial, the sponsor pays for a number of required services and activities (e.g., patient enrollment, informed consent process, certain medical tests or services, reporting of adverse events, IRB fees, data collection and analysis) and expects to receive case report forms, adverse events reports, and other specific data on subjects, all of which would be allowed by authorizations and informed consents signed by the subjects. We ask OCR to confirm that this practice, including the payment by a sponsor for the regular costs of the clinical trial, is permissible and does not require a specific statement in the authorization from subjects, in order for this payment to be made.**

We appreciate the careful attention that SACHRP's prior recommendations have received. Thank you for the opportunity to comment.

Sincerely,

[Chair, SACHRP]

ATTACHMENT A: MODELS OF COMPOUND AUTHORIZATION

FOR A CLINICAL TRIAL & BANKING COMPONENT

Model 1: Combined consent/authorization for clinical trial and banking component, with check-boxes for banking option, and one signature

The covered entity uses a combined consent/authorization, in which the authorization elements for the optional banking activity "piggyback" on authorization statements for the clinical trial. In other words, the recitation of authorization elements is not entirely separate for the banking component, but relevant differences for banking authorization are noted. Through check-boxes, an individual is asked for consent and authorization for the clinical trial and for the optional banking research. A single signature would be provided.

For an example, please see the mark-ups to the Authorization on the next page. This Authorization is the sample published in the NIH/OCR guidance entitled "HIPAA Authorization for Research," available at http://privacyruleandresearch.nih.gov/pdf/authorization.pdf. Mark-ups are shown in **bold red CAPS**.

Model 2: Combined consent/authorization form for clinical trial and banking component, with one signature for clinical trial and another signature for banking

The covered entity uses a combined consent/authorization, in which the authorization has two sections: one for the clinical trial, and one for the optional banking research (*e.g.*, in a separate paragraph or section). An individual is asked for consent and authorization for the clinical trial and the optional banking research. Separate signatures are requested.

Model 3: Combined consent/authorization form for clinical trial and banking component, with check boxes for banking option, but with detailed information about banking presented in a separate brochure or information sheet

The covered entity uses a combined consent/authorization form for a clinical trial with an optional banking component. As part of the IRB-approved informed consent process, the covered entity gives individuals an informational brochure that describes banking research, including in part whether identifiable health information will be used or shared and for what purposes. **The consent/authorization form notes that detailed information will be provided in a separate informational brochure.** The consent/authorization, together with the informational brochure, meaningfully inform individuals of the banking option. An individual is asked for consent/authorization to the clinical trial and optional banking component. A single signature would be provided.

SAMPLE AUTHORIZATION LANGUAGE FOR RESEARCH USES AND DISCLOSURES OF INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION BY A COVERED HEALTH CARE PROVIDER

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study AND OPTIONAL BANKING STUDY

REQUIRED ELEMENTS:

If you sign this document, you give permission to [name or other identification of specific health care provider(s) or description of classes of persons, e.g., all doctors, all health care providers] at [name of covered entity or entities] to use or disclose (release) your health information that identifies you for the research study described below:

[Provide a description of the research study, such as the title and purpose of the research.][ADD OPTIONAL BANKING STUDY]

The health information that we may use or disclose (release) for this research includes [complete as appropriate]:

[Provide a description of information to be used or disclosed for the research project. This may include, for example, all information in a medical record, results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.][STATE WHETHER INFORMATION IS THE SAME OR DIFFERENT FOR THE OPTIONAL COMPONENT]

The health information listed above may be used by and/or disclosed (released) to:

[Name or class of persons involved in the research; i.e., researchers and their staff]

[*Footnote to the Template provides additional examples of who may have access to PHI for the study, including but not limited to research collaborators, sponsors, data coordinating centers, IRBs, Data Safety and Monitoring Boards, and any other entity [or governmental party] to whom the covered entity is expected to make the disclosure.]*

[FOR THE BANKING COMPONENT, INCLUDE WHO MAY USE PHI AND TO WHOM PHI MAY BE DISCLOSED]

[Name of covered entity] is required by law to protect your health information. By signing this document, you authorize [name of covered entity] to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. Please note that [include the appropriate statement]:

- You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment **IN THE CLINICAL TRIAL.**
  (When the research involves treatment and is conducted by the covered entity or

when the covered entity provides health care solely for the purpose of creating protected health information to disclose to a researcher)

- **IF YOU WANT TO ALLOW YOUR HEALTH INFORMATION TO BE USED OR SHARED FOR THE OPTIONAL BANKING RESEARCH, THEN PLEASE SELECT THE CHOICE BELOW THAT INCLUDES BANKING. IF YOU DO NOT AUTHORIZE THE BANKING RESEARCH, YOU MAY STILL PARTICIPATE IN THE CLINICAL TRIAL.**

- [Name of covered entity] may not condition (withhold or refuse) treating you on whether you sign this Authorization.
  (When the research does <u>not</u> involve research-related treatment by the covered entity or when the covered entity is <u>not</u> providing health care solely for the purpose of creating protected health information to disclose to a researcher)

Please note that [include the appropriate statement]

- You may change your mind and revoke (take back) this Authorization at any time, except to the extent that [name of covered entity(ies)] has already acted based on this Authorization. To revoke this Authorization, you must write to: [name of the covered entity(ies) and contact information].
  (Where the research study is conducted by an entity other than the covered entity)
- You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, [name or class of persons at the covered entity involved in the research] may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to: [name of the covered entity(ies) and contact information].
  (Where the research study is conducted by the covered entity)

  [FOR BANKING COMPONENT, ADD CONTACTS IF DIFFERENT]

- **IF YOU AUTHORIZE YOUR HEALTH INFORMATION TO BE USED AND SHARED FOR BOTH THE CLINICAL TRIAL AND BANKING, AND LATER REVOKE YOUR AUTHORIZATION FOR ONLY ONE OF THESE ACTIVITIES, THIS AUTHORIZATION WILL REMAIN IN EFFECT FOR THE OTHER ACTIVITY**.

This Authorization does not have an expiration date [or as appropriate, insert expiration date or event, such as "end of the research study."] **[ADDRESS WHETHER EXPIRATION DIFFERS FOR BANKING COMPONENT]**

[ADD CHECK-BOXES OR OTHER MEANS TO CLARIFY WHETHER INDIVIDUAL IS AUTHORIZING THE CLINICAL TRIAL AND BANKING, OR ONLY THE CLINICAL TRIAL]

_____

Signature of participant or participant’s personal representative

_____

Printed name of participant or participant’s personal representative

_____

Date

_____

If applicable, a description of the personal representative’s authority to sign for the participant.

Attachment C.
Comments and Recommendations Regarding IRB Membership and Definition of Scientist and Nonscientist under 45 CFR 46 and 21 CFR 56 (As Presented)

[DRAFT - 6 Oct 2010]

To: Secretary's Advisory Committee on Human Research Protections (SACHRP)

From: SACHRP Subcommittee on Harmonization (SOH)

Subcommittee on Harmonization Comments and Recommendations regarding IRB membership and definition of Scientist and Non-Scientist under 45 CFR 46 and 21 CFR 56

Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations both include the requirement that IRB membership include "at least one member whose primary concerns are in [the] scientific area[s] and at least one member whose primary concerns are in nonscientific areas."[9] Despite essentially identical regulatory wording, OHRP and FDA guidance documents differ regarding the definitions and examples of "scientist" and "non-scientist." OHRP addresses the issue at OHRP IRB Registration FAQ # 12, on-line at http://www.hhs.gov/ohrp/IRBfaq.html#q12[10]. FDA guidance is found at FAQ # 17 of its Clinical Trial Information Sheet Guidance, on-line at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm115632.htm#IRBMember.[11]

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[9] *HHS regulations at 45 CFR 46.107(c):* Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
FDA regulations at 21 CFR 56.107(c): Each IRB shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in nonscientific areas.

[10] [OHRP] The following are some general guidelines to assist you in composing the IRB membership roster. Scientist/Nonscientist - Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline should be considered a nonscientist. In addition, the IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

[11] [FDA] Which IRB members should be considered to be scientists and non-scientists?
21 CFR 56.107(c) requires at least one member of the IRB to have primary concerns in the scientific area and at least one to have primary concerns in the non-scientific area. Most IRBs include physicians and Ph.D. level physical or biological scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR 56.107(f).

This membership requirement is relevant not only to the composition of the IRB, but also to the review and approval process, since HHS and FDA regulations both specify that a quorum at a convened IRB meeting must include at least one member whose primary concerns are in non-scientific areas.[12]

In the interests of harmonizing OHRP and FDA guidance, and to assist IRBs in appointing appropriately qualified members and adhering to quorum requirements, while still respecting the flexibility implied in the regulatory language, the SOH makes the following recommendations regarding the definitions of scientist and non-scientist:

- OHRP and FDA should issue a single joint guidance on this issue so that IRBs have a single source of information regarding the agencies' viewpoint on this issue. This will facilitate compliance and reduce administrative burden on IRBs.

- The joint guidance should outline accepted criteria for determining whether an IRB member is to be classified as a "scientific" or "non-scientific" member, regardless of whether the individual is serving on a biomedical or a behavioral/social science IRB, and should also allow reasonable flexibility in the interpretation of an individual's "primary concerns," as referenced in the regulations. Examples of clearly-defined scientific members (practicing physician or nurse, Ph.D. level bench scientist, medical laboratory technician, etc.) and clearly-defined non-scientific members (attorney, clergy member, ethicist, etc.) should be given, as well as examples of less clearly-defined but potentially justifiable assignments. The guidance should reference the expectation that institutions that choose to categorize an individual as a non-scientist, when the rationale for the categorization is not apparent based on occupation or training, should maintain written documentation of the reason for the categorization.

- The joint guidance should be included as part of the current FAQs regarding the Electronic Submission System for IRB registration, or should otherwise be posted in conjunction with the IRB registration system, since IRBs that review research regulated by either or both HHS and FDA are required to register using this system.

FDA believes the intent of the requirement for diversity of disciplines was to include members who had little or no scientific or medical training or experience. Therefore, nurses, pharmacists and other biomedical health professionals should not be regarded to have "primary concerns in the non-scientific area." In the past, lawyers, clergy and ethicists have been cited as examples of persons whose primary concerns would be in non-scientific areas.
Some members have training in both scientific and non-scientific disciplines, such as a J.D., R.N. While such members are of great value to an IRB, other members who are unambiguously non-scientific should be appointed to satisfy the non-scientist requirement.

[12] See 45 CFR 46.108(b) and 21 CFR 56.108(c).

• The joint guidance, regardless of how and where it is published, should include an explicit statement(s) that it is both FDA guidance and OHRP guidance. This will ensure that institutions, IRBs, sponsors, and agency employees are aware that it represents the agencies' current thinking on the topic.

Discussion

The existing OHRP FAQ states that an IRB member should be considered a non-scientist if that individual's training, background, and occupation "would *incline* [sic] them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline." The FDA FAQ is more restrictive, and advises that only individuals with "little or no scientific or medical training or experience"—whether in the biological or the physical sciences—should be classified as non-scientists. In addition, FDA indicates that individuals with advanced or professional training in both scientific and non-scientific areas should not be classified as non-scientists.

The SACHRP believes that the intent of the regulations was to distinguish between two categories of IRB members:

• Individuals who are professionally conversant with the scientific method (either by virtue of advanced training or by current occupation in scientific fields), and who might thus be *inclined* to view a research protocol primarily from the viewpoint of a scientist; and

• Individuals who lack professional scientific training and do not work in scientific areas, or who may have past scientific training but who have worked only in areas that do not exercise that training, and might thus be *inclined* to view a research protocol primarily from the viewpoint of a non-scientist.

SACHRP believes the scientist/non-scientist distinction was designed to ensure a range of intellectual and philosophical perspectives among IRB members. By use of the term "primary concerns," both OHRP and FDA regulations acknowledge that the concerns of an IRB member are unlikely to lie *solely* in scientific, or *solely* in non-scientific, areas.

For instance, an institution might choose to appoint a long-time elementary school teacher with prior advanced training in psychology as a non-scientific member, or an attorney specializing in biomedical intellectual property law as a scientific member. We believe that such appointments, with appropriate justification, are consistent with regulatory intent and should be allowed.

The current FDA guidance states that an IRB member with professional training in both scientific and non-scientific disciplines, such as a J.D., R.N., does not meet the non-scientist

requirement. While this analysis would ordinarily prevail, individuals' circumstances may vary, and we believe that there should not be a flat exclusion of such individuals from the non-scientist category, if the institution has and maintains justification for such an assignment. Similarly, an individual with a bachelor's or associate degree in a scientific area, but who does not and has not subsequently worked in a scientific area, could appropriately be classified as a non-scientific member.

The current OHRP guidance seems to indicate that for the purpose of IRB member designation, scientists are limited to being either behavioral or biomedical scientists. In accordance with the above discussion, we believe that scientists in fields other than behavioral or biomedical sciences, such as geology or statistics, should be considered scientists for the purpose of IRB membership designation.

Finally, and to reinforce the concept of harmonization, we believe that the joint guidance should clarify that the concepts of scientist and non-scientist should ordinarily not vary from behavioral to medical IRBs. For instance, an anthropologist should be considered a scientist on both a behavioral and a medical IRB, rather than being considered a scientist for a behavioral IRB and a non-scientist for a medical IRB.

We hope that these comments and recommendations will promote regulatory harmonization and reduce administrative burden for the regulated research community, by clarifying a common standard for IRBs reviewing research subject to HHS and FDA oversight, while allowing a reasonable degree of local flexibility in meeting both the requirement and intent of the regulations.

Sincerely,

Attachment D.
Comments and Recommendations Regarding IRB Membership and Definition of Scientist and Nonscientist under 45 CFR 46 and 21 CFR 56 (As Approved)

~~**From: SACHRP Subcommittee on Harmonization**~~

From: Secretary's Advisory Committee on Human Research Protections (SACHRP)

~~**Subcommittee on Harmonization**~~ ***Comments and Recommendations regarding IRB membership and definition of Scientist and Non-Scientist under 45 CFR 46 and 21 CFR 56***

Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations both include the requirement that IRB membership include "at least one member whose primary concerns are in [the] scientific area[s] and at least one member whose primary concerns are in nonscientific areas."[13] Despite essentially identical regulatory wording, OHRP and FDA guidance documents differ regarding the definitions and examples of "scientist" and "non-scientist." OHRP addresses the issue at OHRP IRB Registration FAQ # 12, on-line at http://www.hhs.gov/ohrp/IRBfaq.html#q12[14]. FDA guidance is found at FAQ # 17 of its Clinical Trial Information Sheet Guidance, on-line at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm115632.htm#IRBMember.[15]

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[13] *HHS regulations at 45 CFR 46.107(c):* Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
FDA regulations at 21 CFR 56.107(c): Each IRB shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in nonscientific areas.

[14] [OHRP] The following are some general guidelines to assist you in composing the IRB membership roster. Scientist/Nonscientist - Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline should be considered a nonscientist. In addition, the IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

[15] [FDA] Which IRB members should be considered to be scientists and non-scientists?
21 CFR 56.107(c) requires at least one member of the IRB to have primary concerns in the scientific area and at least one to have primary concerns in the non-scientific area. Most IRBs include physicians and Ph.D. level physical or biological scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR 56.107(f).
FDA believes the intent of the requirement for diversity of disciplines was to include members who had little or no scientific or medical training or experience. Therefore, nurses, pharmacists and other biomedical health professionals should not be regarded to have "primary concerns in the non-scientific area." In the past, lawyers, clergy and ethicists have been cited as examples of persons whose primary concerns would be in non-scientific areas.

This membership requirement is relevant not only to the composition of the IRB, but also to the review and approval process, since HHS and FDA regulations both specify that a quorum at a convened IRB meeting must include at least one member whose primary concerns are in non-scientific areas.[16]

In the interests of harmonizing OHRP and FDA guidance, and to assist IRBs in appointing appropriately qualified members and adhering to quorum requirements, while still respecting the flexibility implied in the regulatory language, the SACHRP makes the following recommendations regarding the definitions of scientist and non-scientist:

- OHRP and FDA should issue a single joint guidance on this issue so that IRBs have a single source of information regarding the agencies' viewpoint on this issue. This will facilitate compliance and reduce administrative burden on IRBs.

- The joint guidance should outline ~~accepted criteria~~ **general principles** for determining whether an IRB member is to be classified as a "scientific" or "non-scientific" member, regardless of whether the individual is serving on a biomedical or a behavioral/social science IRB, and should also allow reasonable flexibility in the interpretation of an individual's "primary concerns," as referenced in the regulations. **These principles should indicate that the requirement for having a "nonscientific" member lies in the need to have at least one representative on the IRB who is not self-identified with those conducting research that will be reviewed by the IRB.** Examples of ~~clearly-defined~~ scientific members (practicing physician or nurse, Ph.D. level bench scientist, medical laboratory technician, etc.) and clearly-defined non-scientific members (attorney, clergy member, ethicist, etc.) should be given, as well as examples of less **well** ~~clearly-~~defined but potentially justifiable assignments. The guidance should reference the expectation that institutions that choose to categorize an individual as a non-scientist, when the rationale for the categorization is not apparent based on occupation or training, should maintain written documentation of the reason for the categorization.

(The remainder of the letter is unrevised, with the exception that references to SOH will be changed to SACHRP.)

Some members have training in both scientific and non-scientific disciplines, such as a J.D., R.N. While such members are of great value to an IRB, other members who are unambiguously non-scientific should be appointed to satisfy the non-scientist requirement.

[16] See 45 CFR 46.108(b) and 21 CFR 56.108(c).

Attachment E.
Preface to FAQs on Biospecimens (As Approved)

Preface to SACHRP FAQs on Informed Consent and Research Use of Biospecimens

The collection and use of human specimens have become essential to biomedical research. These biospecimens include blood and other tissues, some collected originally for clinical lab tests, some removed during surgeries, and some obtained specifically for research. While there is no accurate catalog of the number or locations of specimens, there are reasonable estimates that billions of specimens are now stored in laboratories, repositories and "tissue banks" across the country. Coupled with associated clinical data and the power of bioinformatics, these specimens represent an invaluable resource for current and future research on human health and disease.

At the same time, there are significant ethical, legal and social policy implications relating to the collection, storage and use of biospecimens. Institutions, investigators, institutional review boards (IRBs), funding agencies and the public are struggling with issues like informed consent, ownership, **stewardship,** genetic testing, and future uses that are often unspecified at the time specimens are first obtained. The **ethical t**ensions that frequently exist between the needs of science and the rights of individuals are **present in** ~~if anything, accentuated by~~ research involving specimens, and there is much inconsistency and uncertainty as to how they should be used responsibly. The research community would benefit from federal-level guidance.

The Secretary's Advisory Committee on Human Research Protections (SACHRP) has considered a number of unanswered questions relating to informed consent and research use of biospecimens. Upon request by SACHRP, the Subpart A Subcommittee of SACHRP deliberated on these issues and presented their recommendations to SACHRP for further discussion and approval, over the course of several meetings in 2009 and 2010. The finalized recommendations take the form of a series of "Frequently Asked Questions" (FAQs), each presented as a commonly-encountered scenario and a suggested response that addresses regulatory and ethical issues. The goal was to provide a framework for IRBs, institutions and investigators to consider individual research scenarios without proscribing the final outcome, recognizing that those decisions will always be case-specific.

It is hoped that these compiled FAQs constitute a product that the Office for Human Research Protections (OHRP) and others can use to provide much-needed guidance in this area.

Secretary's Advisory Committee on Human Research Protections

October 19 and 20, 2010
Washington, D.C.

Certification of the Summary of Minutes

I hereby certify that, to the best of my knowledge, the foregoing summary of minutes is accurate and complete.

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Barbara Bierer, M.D., Chair Date